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A.M.A. ARCHIVES OF NEUROLOGY & PSYCHIATRY

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New York Academy of Medicine, Section of Neurology and Psychiatry, and New York Neurological Society

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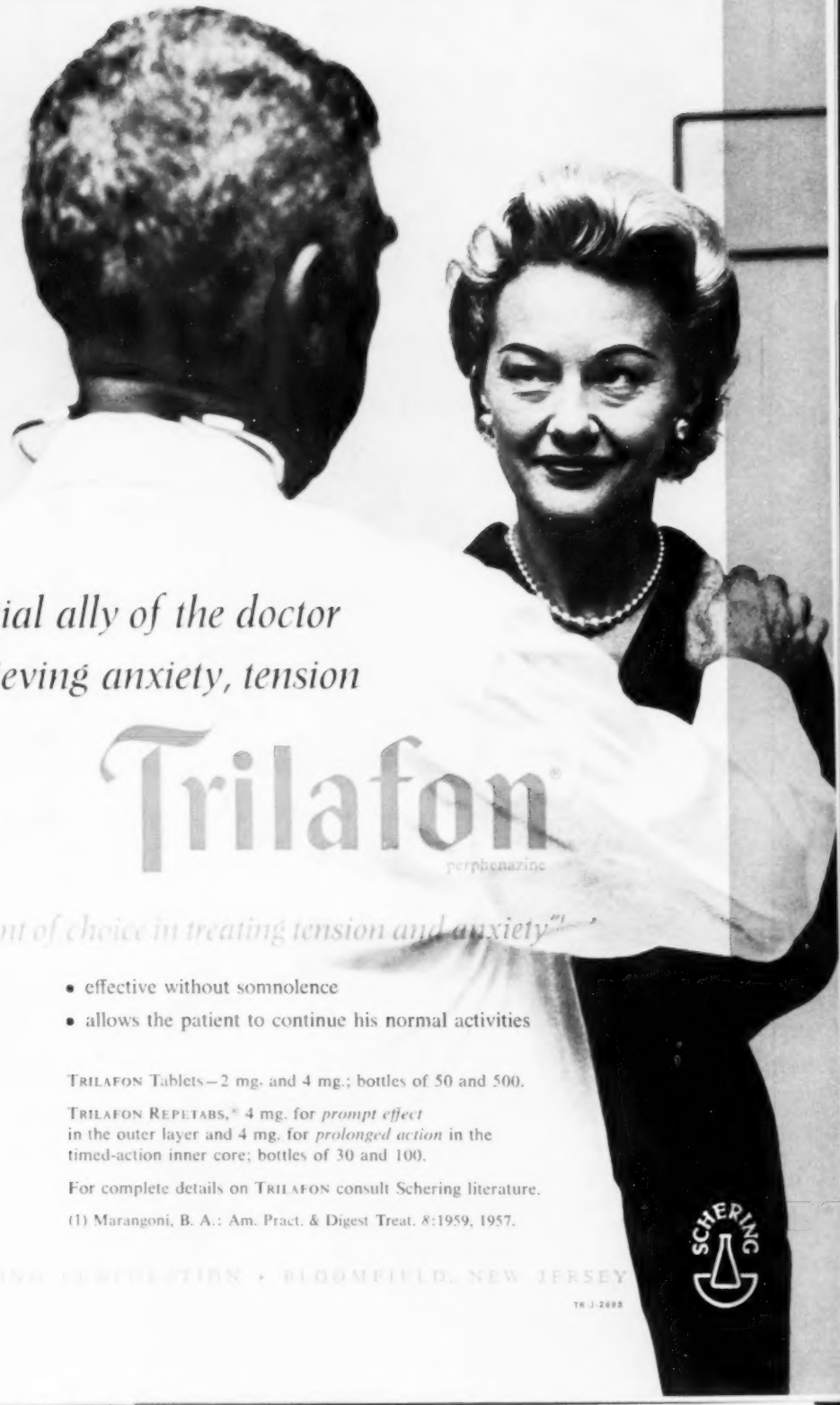

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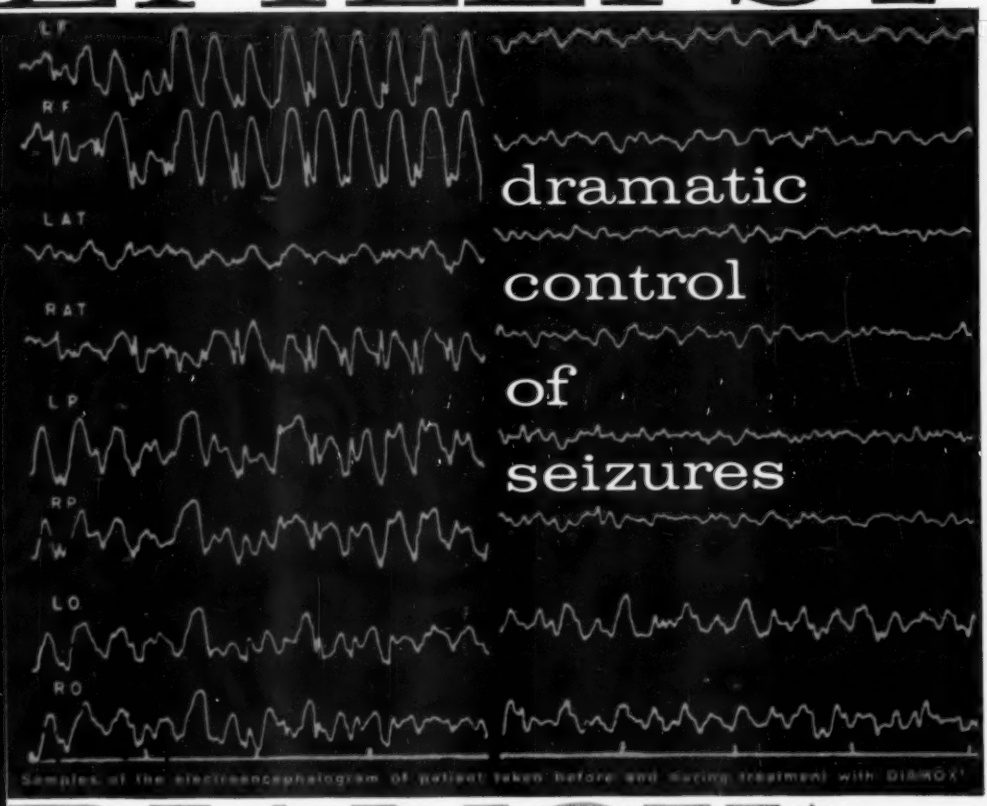

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1. Lombroso, C. T., Davidson Jr., D. T., and Grossi-Bianchi, M. L.: Further Evaluation of Acetazolamide (DIAMOX) in Treatment of Epilepsy, J.A.M.A. 160:268-272, 1956.

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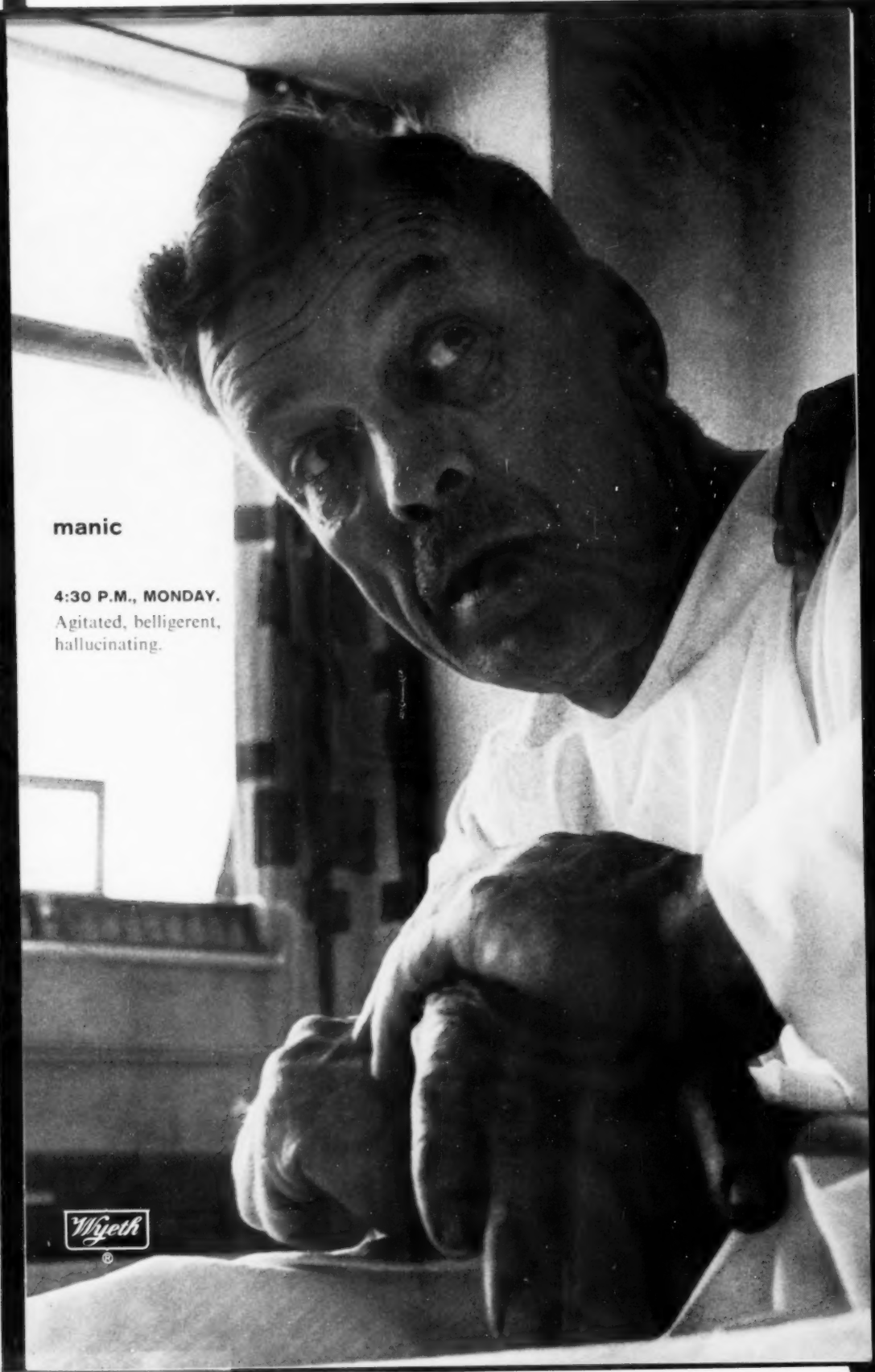
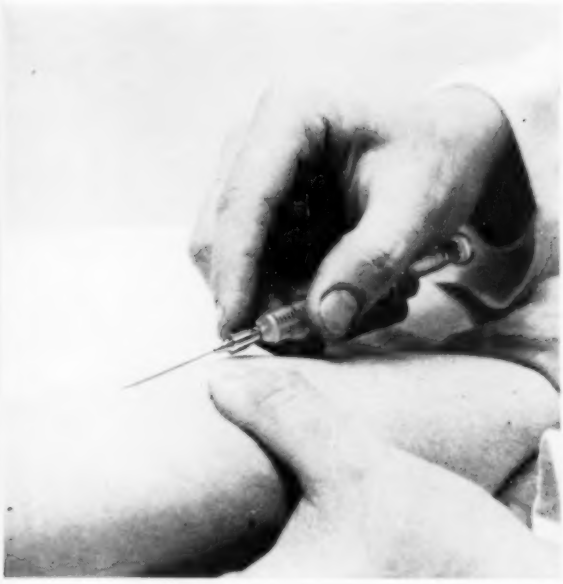
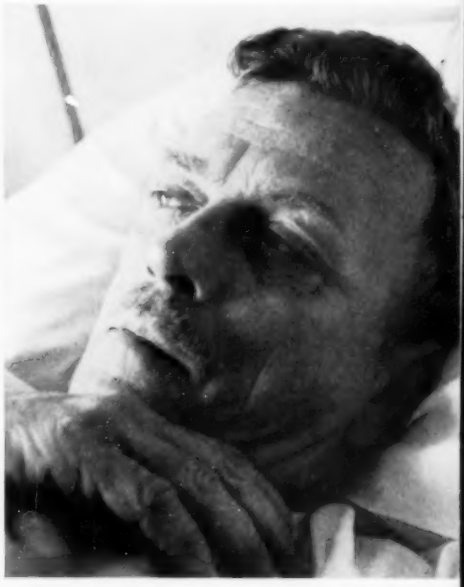

manic
4:30 P.M., MONDAY.
Agitated, belligerent, hallucinating.
Wyeth

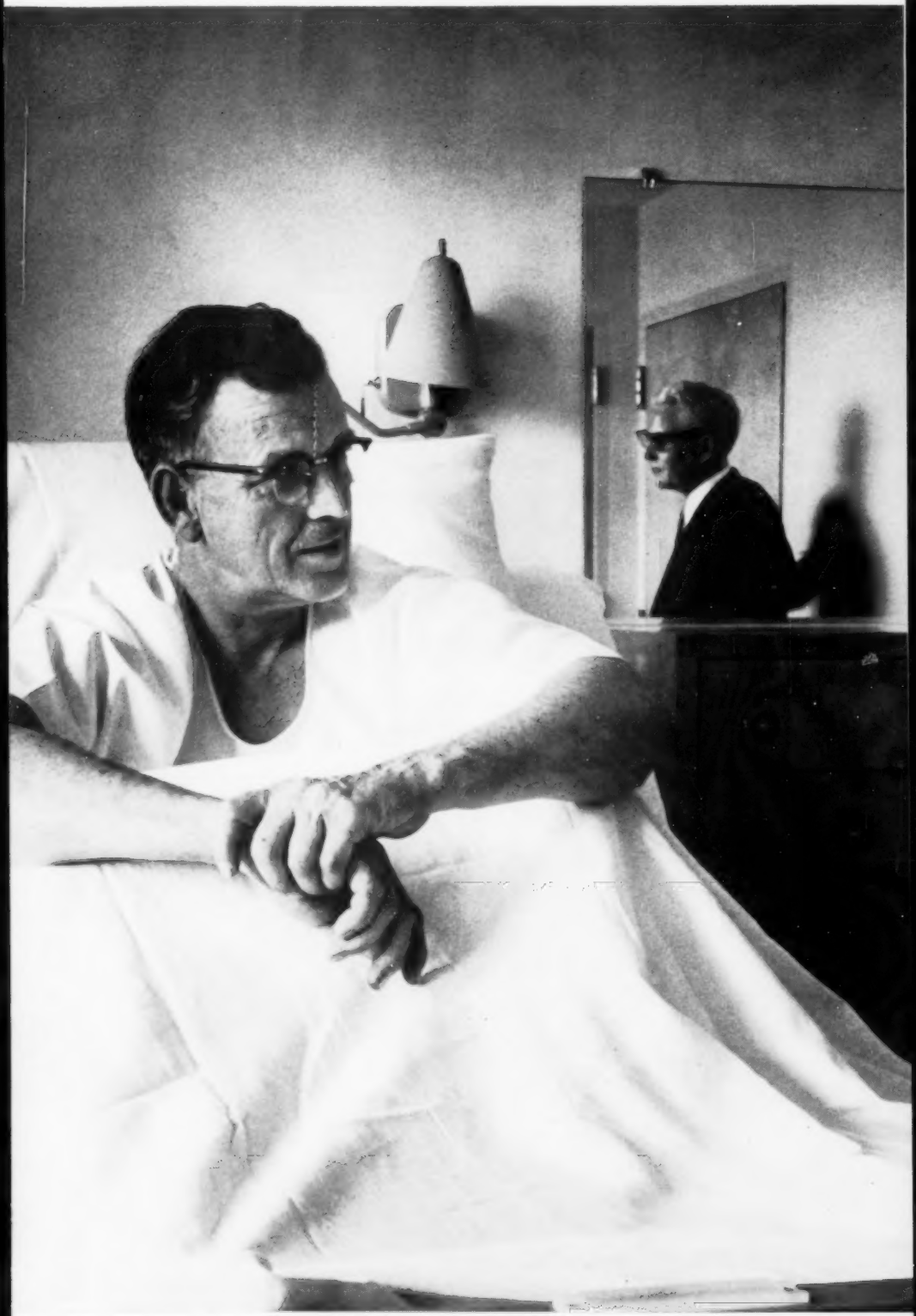
4:40 P.M., MONDAY. SPARINE I.V.



5:00 P.M., MONDAY. Calmer, less hostile. cooperatively to questions.



7:30 A.M., TUESDAY. Refreshed but some agitation remains. SPARINE I.V.



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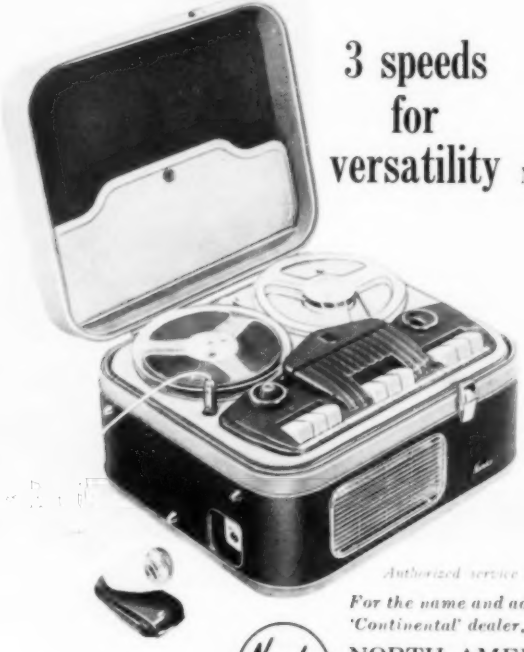

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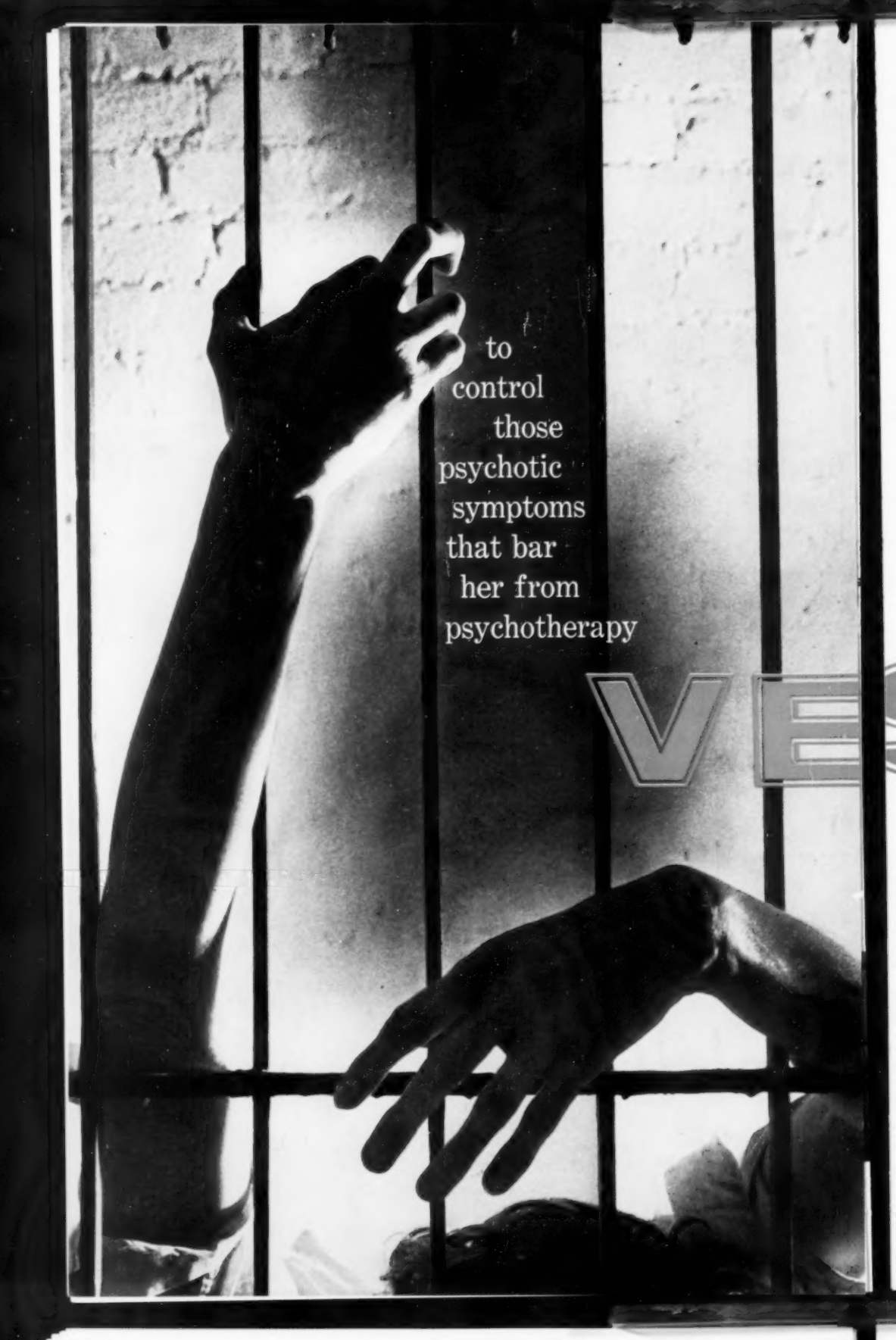
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1. Graffagnino, P. N., Friel, P. B. and Zeller, W. W.: Emotional disorders treated with meprobamate and promazine. Connecticut M. J. 21:1047, Dec. 1957.

SYMPTOMATIC IMPROVEMENT

(hospitalized patients—all types)

by disease

DIAGNOSIS	NO. OF PATIENTS	NO. IMPROVED
SCHIZOPHRENIA		
PARANOID	7	2
NON-PARANOID	45	34
DEPRESSION		
PSYCHOTIC†	37	25
NEUROTIC	16	10
ANXIETY STATE	9	8
CHARACTER DISORDERS	15	13
OTHERS	16	13
TOTALS	145	105

by symptom

SYMPTOM	NO. IMPROVED
SLEEP DISTURBANCES	36
ANXIETY	30
TENSION	31
AGITATION	8
OTHERS	11
TOTAL	116

†Relief mainly in symptoms of anxiety, tension and insomnia.

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Specific and General Effects of Brain Injury in Man

Evidence of Both from a Single Task

HANS-LUKAS TEUBER, Ph.D., and ROBERT S. LIEBERT, M.A., New York

Introduction

In several reports from this laboratory,[4,7,8] it has been pointed out that penetrating brain wounds in man tend to have twofold effects on behavior: specific effects, restricted to cases of injury in certain locations,[4,5] and general effects, which appear after injuries, irrespective of their site.[6,8] Until now, separate tasks have been necessary to demonstrate either kind of effect; the present report deals with a single experimental situation yielding evidence for both.

The experiment is based on a classical perceptual task (first used by Aubert in 1861), that of setting a luminous line to the apparent vertical when the subject is tilted in a dark room.[1,2] Under conditions of moderate body tilt (up to 30 degrees) to his right, a normal adult makes constant errors by setting the line too far to the left of the plumb line, and conversely for body tilts to the left. In a previous study,[5] we have shown that these constant errors are specifically enhanced by brain injury involving the anterior (frontal) regions.

The additional analysis of this experiment was suggested to us by the work of Werner and Wapner and their collaborators,[3,9,10] who have used the Aubert phenomenon and its variants extensively in the study of perceptual processes in normal children,[9] in adults,[10] and in various pathologic states.[3] In analyzing their subjects' settings of the visual vertical under conditions of body tilt, Werner and Wapner[10] have distinguished two types of error: They have described the usual constant error, which in normal adults consists of setting the luminous line slightly too far to the right when the body is tilted moderately to the left, and conversely. This is the type of error employed by us in our study of the phenomenon in brain-injured subjects.[5]

However, Werner and Wapner analyze their data in still another way—by extracting a "starting position effect" (SP effect).[10] This effect is observed by noting to what extent the subject displaces the luminous line in the direction in which it was presented at the beginning of an individual trial.

This SP effect turned out to be maximal in normal children, decreasing gradually in extent until late adolescence.[9] In normal adults the SP effect is somewhat more marked when the subject is under the influence of the drug lysergic acid diethylamide (LSD-25) than under placebo conditions.[3] Adult schizophrenics tend to show somewhat larger SP effects than normal

Received for publication June 22, 1957.

New York University-Bellevue Medical Center.

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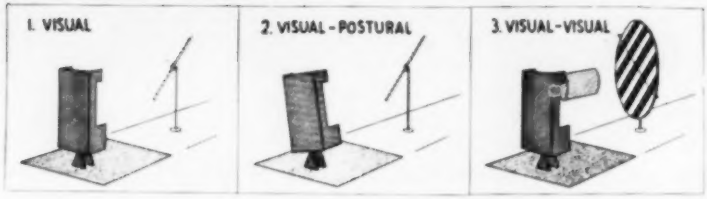

Fig. 1.—Schematic diagrams showing the three experiments in the order in which they were performed.

controls, and when these schizophrenic patients are given LSD-25, their SP' effects are significantly increased.[3]

In view of this sensitivity of SP' effects to various group differences, we decided to reinvestigate the results of our earlier experiments employing the Aubert phenomenon and its variants,[5] and to compare the constant errors of settings with the SP' effects.

Procedure and Subjects

The experimental methods and subjects are described in detail in an earlier publication.[5] There were three experiments, performed in series, usually within a single session.

Experiments I and II.—Briefly, each subject was asked to set a luminous line (1 meter in length, 2 cm. in width) to the vertical. The line was placed at a distance of 2 meters from the subject, in his frontal plane, and could be rotated in that plane in either direction, around its midpoint. In 18 consecutive trials, the subject set the line to the subjective vertical, with the initial position of the line alternately 28 degrees to the left or to the right. On the first six of these trials the subject's body was upright (Experiment I, Fig. 1, *1*). On the next six trials he was tilted in the chair 28 degrees to his left, and on the last six trials, 28 degrees to his right. These 12 trials constituted Experiment II (Fig. 1, *2*).

Experiment III.—After a rest period, the subject was seated again upright and was asked to set a black thread (1 meter in length) to the subjective vertical (Experiment III). The thread appeared in his frontal plane at a distance of 2 meters and could be moved in front of a 1-meter-diameter disk with black and white stripes (5 cm. in width). The display was viewed through a tube, so that the subject could see nothing but the striped disk with the black thread in front of it (Fig. 1, *3*). There were 12 consecutive trials in Experiment III, with initial position of the black thread alternately 28 degrees to the left and to the right. For the first six trials, the striped field was placed so that the stripes ran at a 28 degree angle through the subject's field to his left, and for the remaining six trials of Experiment III, the stripes ran 28 degrees to the subject's right.

The present analysis of results is based on data from 72 subjects for Experiments I and II, viz., 26 controls (men with peripheral nerve injury, but without brain wounds); 24 men with proved penetration, by missile, of the anterior third of the brain, and 22 men with similar penetration of the posterior third. Sixty-two of these subjects participated in Experiment III, viz., 21 of the controls, 24 with anterior brain lesions, and 17 with posterior brain lesions.

Results

Constant Errors.—In the earlier analysis,[5] it was found that constant errors of setting were quite small in Experiment I (setting the luminous line with body upright); there were no significant differences among groups. In Experiment II (setting the luminous line with body tilted), all groups showed constant errors of setting, by placing the line too far to the left of vertical when the body was tilted right, and conversely. However, the group with frontal lesions showed this constant error to a significantly larger extent than did the group with posterior lesions, which did not

differ from the controls. In Experiment III, constant errors of setting appeared in all groups. The errors consisted in placing the black thread slightly off vertical, in the direction of the stripes. However, the posterior-lesion group made larger constant errors than did those with anterior lesions or the controls.*

Starting-Position Effects.—Average starting-position effects were determined as follows: The subject's setting of the luminous line or black thread was considered separately for all trials in which the line was first presented 28 degrees to the left (left SP) and for all trials in which it was presented 28 degrees to the right (right SP). If the subject's setting deviated from the objective vertical in the direction of the SP of the line, the score (in degrees of arc) was recorded as positive; wherever the setting was to that side of the objective vertical which was opposite the SP, the score (in degrees of arc) was recorded as negative. All scores for a given subject, in a given experiment, were then added algebraically and averaged.

The mean starting-position effects were assessed by a series of analyses of variance, performed separately for each of the three experiments. For each experiment, the following groups of subjects were compared with one another:

(*a*) Controls *vs.* left anterior lesions *vs.* right anterior lesions *vs.* bilateral anterior lesions *vs.* left posterior lesions *vs.* right posterior lesions *vs.* bilateral posterior lesions

(*b*) Controls *vs.* left-hemisphere lesions *vs.* right-hemisphere lesions *vs.* bilateral lesions

(*c*) Controls *vs.* anterior lesions (either or both hemispheres) *vs.* posterior lesions (either or both hemispheres)

(*d*) Controls *vs.* all brain-injured patients

Starting-position effects, for all groups, computed in this fashion, were quite small (about one-half of a degree) as long as the subject's body was upright (Experiment I); there were no significant differences between controls (without brain injury) and any of the brain-injured subgroups, or all brain-injured subjects combined.

In contrast, as soon as the subject was tilted to the left or right (Experiment II), marked SP effects appeared in all groups, controls as well as brain-injured subjects. There was no significant difference due to the direction of the body tilt (although tilts to the left seemed to produce slightly greater SP errors than the subsequent tilt to the right); nor did any group react differentially to the direction of body tilt. Throughout, however, the brain-injured groups showed larger SP effects when tilted than did the controls. While there were no significant differences among brain-injured subgroups [in any of the analyses—(*a*), (*b*), and (*c*)—above], the brain-injured group as a whole was clearly different from the control population [analysis (*d*)] in showing significantly larger SP effects in setting the line while the subject's body was tilted (Fig. 2).

These differences did not appear in the final experiment (Experiment III), in which the subject, while upright, had to set a black thread to the vertical, with the thread appearing against an obliquely striped background. In this situation no group (neither controls nor brain-injured) showed significant SP effects.

Comment

The analyses just reported indicate that SP effects are enhanced in the presence of brain injury, and that they are enhanced irrespective of the presumed site of the lesion. In this respect, the SP effects in the Aubert experiment are nonspecific

* Together, the evidence from the two experiments (luminous line and striped field) yields what may be called "double dissociation" of symptoms, since on one variation of the task the subjects with frontal lesions, but not those with parietal lesions, were maximally affected, and on the other variation the converse was true.[15] The results were thus specific (i. e., localizable) sequelae of penetrating brain wounds. Nevertheless, the specific effects coexisted in the same patients with general (nonlocalizable) effects: On different tasks, such as a hidden-figure test,[6] all groups of brain-injured men, regardless of location of lesion, were inferior to the controls.

*Summary of Analysis of Variance (Experiment II)**

Source	SS	d. f.	Mean Square	F	P
Between Ss	1088.27	71	15.47		
Between groups	66.46	1	66.46	4.50	<0.05
Between Ss in same group	1031.81	70	14.74		
Within Ss	381.62	72	5.30		
Between tilts	7.96	1	7.96	1.49	>0.05
Tilt × group	0.02	1	0.02	0.004	>0.05
Pooled Ss × tilts × group	373.64	70	5.34		
Total	1470.89	143	10.35		

* Body tilt × starting positions (controls vs. brain-injured subjects).

(nonlocalizable) sequelae of brain injury, in contrast to the constant errors of setting reported earlier, which are maximal for men with anterior cerebral lesions, on the Aubert task, and maximal for men with posterior lesions on the line-and-striped-field task.[5] Depending on the method of analyzing results, the Aubert task thus yields specific (localizable) signs (constant errors) and nonspecific (general) signs (SP effects).

We must stress the conditions under which this twofold result appears: Within the array of tasks used, the necessary conditions for obtaining specific as well as general effects, on the same test, involve a visual setting (luminous line) under conditions of abnormal body posture (left or right tilt) on the subject's part. Only when the body was tilted, did our subjects (all groups) show large SP effects. Only when tilted, did the SP effects of the brain-injured as a group exceed those of the controls without brain injury. Abnormal posture, in its interaction with the visual task, had to be present to reveal SP effects, and to make these effects differential for brain-injured and controls. In the final task—the setting of a thread to the vertical against an obliquely striped field when the subject's body was upright—no significant SP effects appeared in any group.

Starting-position effects under conditions of body tilt in the Aubert task can thus be classified with various other general or nonspecific effects of brain injury: the abnormal difficulty presented to the brain-injured by hidden-figure tasks[8] or by certain form-board tests.[6] It must be realized, however, that the abnormal SP effects are nonspecific in the broadest sense: They not only are abnormal irrespective of site of injury but may appear, as one of us (R. L.) has shown, in certain transient toxic states[3]

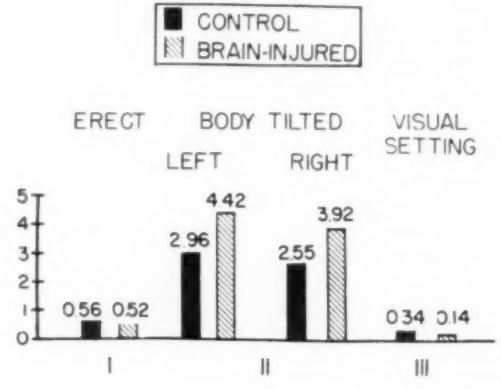

Fig. 2.—Starting-position effects, in degrees of arc, obtained for controls and brain-injured subjects in Experiments I, II, and III.

and in adult schizophrenics. Similarly, large SP effects are the norm in healthy children,[9] so that it is clear that we are dealing here with a rather general phenomenon. For theoretical reasons, however, it remains remarkable that one and the same task—the Aubert task—could be made to yield general and specific signs of cerebral lesion.

Summary and Conclusions

When a normal adult attempts to set a luminous line to the vertical, in a dark room, the setting will be quite accurate as long as the subject's body is upright; when the subject is tilted moderately (28 degrees) to his left, he tends to err by setting the vertical to the right of the plumb line, and conversely for body tilts to the right. These constant errors of setting have previously been shown to be abnormally enhanced after frontal brain injury, thus constituting a relatively "specific" (localizable) effect of brain injury in man.

The present study adds the observation that the same task (differently analyzed) reveals general (nonlocalizable) effects of brain injury (coexisting with more specific kinds of effects): Brain-injured adults with lesions in any lobe, in either hemisphere, show abnormally large "starting-position errors." Such SP effects are found by noting the subjects' tendency to set the luminous line somewhat farther to the left when the line is moved in from a SP on the subject's left (30 degrees), and farther to the right when the line is moved in from the subject's right (30 degrees).

The subjects were 46 adults with penetrating brain wounds and 26 controls (adults with wounds of peripheral nerves, but not of the brain). As long as the luminous line was set in the dark while the subject's body was upright, no significant SP effects appeared; but when the subject's body was tilted (28 degrees right or left), marked SP effects appeared in all groups (brain-injured and controls). The failure of SP effects to appear in the upright position suggests that interaction between visual settings and abnormal posture is a necessary condition for obtaining SP effects on this task.

However, SP errors in the brain-injured groups exceeded those in the controls to a significant extent, although no subgroup among the brain-injured (classified by site of penetration into the brain) revealed any differential effect in this respect. Thus, one and the same task could be shown to reveal general (nonlocalizable) and specific (relatively localizable) effects of brain injury in man.

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Recall with Amobarbital (Amytal) Sodium in Diagnosis of Seizures

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The differential diagnosis of generalized seizures and psychogenic-seizure-like spells is one of the common and difficult problems a clinical neurologist encounters. The electroencephalogram, unfortunately, does not always solve the problem. Furthermore, evidence that a patient has emotional problems does not necessarily rule out epilepsy. The problem may be particularly difficult in military service, where witnesses of a patient's spells may be thousands of miles from the hospital to which he has been transferred.

It is most important to differentiate psychogenic-seizure-like episodes from seizures. The patient with psychogenic episodes which are mistakenly diagnosed as true convulsive seizures may undergo unnecessary diagnostic procedures, be deprived of appropriate psychiatric treatment, continue to have spells in spite of anticonvulsant medication, and, because of his apparent uncontrolled seizure problem (along with his personality disturbances), become a "thorn in the side" of the neurologist. In the military service he may be medically retired and compensated for epilepsy that does not exist.

Peterson et al., in 1950, described the use of hypnosis in the diagnosis of epilepsy, pointing out that an absolute amnesia exists for the period of a generalized seizure and that if under hypnosis a patient demonstrates complete recall for an episode, that episode was not a grand mal seizure.[1] I have had no experience with hypnosis and am reluctant to learn the technique (as are probably most physicians concerned with this problem). It seemed likely, however, that the same information could be obtained with amobarbital (Amytal) sodium.

I have interviewed 60 patients with the use of amobarbital sodium to determine the presence or absence of recall for their spells. The procedure in general was used only in problem cases—those in which little or no description of spells was available, and those in which genuine seizures seemed likely but in which electroencephalograms were normal, some facet of the history suggested a possible psychogenic basis for the spells, or anticonvulsant medication had had no effect on the supposed convulsive disorder. Use of amobarbital sodium established a diagnosis of psychogenic-seizure-like episodes rather than epilepsy in 36 of these 60 problem cases.[2]

To obtain recall, if such is possible, it is necessary to establish good rapport with the patient. If the patient feels that the amobarbital interview is being held to show that he is lying or shirking duty or is worthless, probably nothing will be gained by the interview. The patient is told that he will be given an injection that will make him sleepy, but which perhaps will enable his doctor to help him. Five-tenths gram of amobarbital sodium is dissolved in 10 cc. of water and injected intravenously over a period of 10 minutes, to the point of drowsiness. Occasionally less than 0.5 gm. of amobarbital sodium is required, and occasionally as much as 1.0 gm. is required. During the injection, the patient is casually asked about activities and events beginning several hours before the episode that is to

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be investigated—for example, what he ate for breakfast, with whom he ate, what their conversations were about, what he did at work, and how he felt when he returned from work. As the patient reaches the point of drowsiness, he has arrived in his story to the period immediately preceding the spell and the period of the spell. The patient is asked what he was thinking about, how he was feeling, how his spirits were, how various parts of his body felt, what position he was in, then what happened, etc. He is asked to recall how he fell, what position his legs and arms were in immediately after falling, whether his eyes were open or closed, how he was breathing, how (or whether) he moved his extremities, who was in the room, and what was said and done. A patient may say, "I don't remember," but if he is told to close his eyes and go back to the time of the spell, he may then recall what happened; not infrequently he will repeat the spell. After the examiner has satisfied himself that the patient does or does not demonstrate recall for the episode, then he goes on to another episode. Usually at least the last and first episodes, any that have been witnessed and thought to be true seizures, and (if the previous history suggests more than one kind of spell) at least one example of each kind of spell are discussed.

If the patient does not demonstrate complete recall for an episode, one can draw no definite conclusions in regard to the presence or absence of a convulsive disorder. However, if the patient does demonstrate recall for the entire episode, one can conclude that that episode was not a generalized seizure.

The following cases represent typical examples in which the possibility of generalized seizures existed and in which the use of amobarbital was helpful.

Report of Cases

CASE 1.—A 23-year-old soldier was hospitalized with a diagnosis of epilepsy. For six years he had had one to eight black-out spells a month. He said that he had been told that his arms and legs shook, that he had bitten his tongue once, and that he had been incontinent of urine once. The last episode had occurred four days before admission, at 11 p. m. in a Japanese establishment, where he was talking with a buddy, two Japanese girls, and a proprietress. He had a headache, felt nervous, and after about 10 minutes suddenly blacked out, remembering nothing more until he awoke two hours later, confused and with a headache. A cousin also had black-out spells. Neurological examination was normal. The electroencephalogram was abnormal because of paroxysmal nonfocal 4- to 6-per-second activity.

With the use of amobarbital sodium, the patient recalled in detail the entire episode. He had had a "clanging" in his head for two hours, stood up, stumbled, felt "dizzy in the head," and began to shake his arms; the proprietress asked him to lie down, but he continued to fling his arms about, hitting the wall. The "shaking" continued for a few minutes, and, as he was sitting down, he fell forward to the floor face down and with his arms at his sides. He recalled that his eyes were closed ("my eyes are always closed when I have a spell"), that he continued to fling his arms, that the proprietress, a girl, and his buddy held him down and turned his head to the side, that his friend gave him an aspirin, and that he was then carried to his room, where he went to sleep. (He awoke about an hour later and continued the activities of the evening.) He recalled in detail the next to the last spell, which had occurred under similar circumstances and had been essentially the same. In regard to his first spell, he recalled that at the age of 12 he was sitting at his school desk trying to solve an arithmetic problem. (His cousin, who was a "cripple" and whom he had seen have "fits," was in the same room.) He recalled that the teacher was talking to him, that he had the same "clanging" in his head and felt a little "dizzy in the head," and that he then began to jerk his arms and legs (demonstrating how he flailed his extremities in a nonrhythmical manner). He then put his head down on his desk. There was no loss of consciousness at any time during the episode. He stated that all his spells were exactly the same and denied ever biting his tongue or being incontinent.

CASE 2.—A 25-year-old soldier was transferred to a general hospital with a diagnosis of epilepsy. He had been hit on the head with a rock at the age of 10, had had his first spell one month later, and had had about one spell each month since that time. The spells were said to occur without warning and to be associated with stiffness of the entire body and shaking. He had never wet himself or bitten his tongue but had bitten his lower lip. His father and a cousin were said to have had epilepsy. A note from the transferring hospital stated: "Patient admitted yesterday in a typical convul-

sion, characterized by intermittent rigidity, rough tremors of the right arm, head turned to the left, occasional opisthotonos, and cyanosis, lasting about 15 minutes."

Neurological examination was normal except for limited intellectual endowment. Waking and sleeping electroencephalograms and x-rays of the skull were normal. About one week after admission he had a spell observed and described by a nurse as a "typical grand mal seizure with unconsciousness and tonic and clonic activity."

Four days later, under the influence of amobarbital sodium, the patient demonstrated complete recall for the entire episode. He described much emotional turmoil during the previous week. On the morning of the spell he had not felt like eating breakfast, lay down on his bed, and was thinking about the letter he had received from his wife the day before, "still talking about a divorce." He said: [I felt] "awful—all tore up inside like I just didn't have anything to live for and like I just didn't give a damn about nothing." He began to note pains in his abdomen; his heart "hurt awful bad," and, as he said, "I just couldn't get control of myself." Then his so-called seizure began. He demonstrated in detail how he became stiff all over (as he stiffened his legs out, clenched his fists across his chest, and arched his back and neck), how he jerked (as he demonstrated some gross rhythmical movements with either or both arms but with some quivering movements between the gross movements), how he gasped for breath, and how his eyes were closed tightly. He described how his roommate noticed him and left the room to call a corpsman, who came into the room in about two minutes. He recalled that the corpsman commented, "There is nothing I can do for him except call the nurse," which he did. He recalled the nurse's coming into his room a short time later. One other similar spell was described in detail. He indicated a great deal of preoccupation with death—killing himself, the deaths of people he had known, and how people die. When asked to demonstrate how people die, he stiffened out, arched his back and neck, closed his eyes, jerked his upper extremities, and gasped for breath, showing exactly the same phenomena which he had demonstrated in regard to his so-called seizure.

Case 3.—A 19-year-old soldier was hospitalized because of seizures. During the previous nine months he had had six episodes of loss of consciousness, which were preceded by a blurring of vision and headache for a few seconds. A transferring note described the last spell as follows: "Patient was sitting alongside his bed, stood up, and fell over the bed without crying out. After a minute he became rigid all over and had a generalized clonic convulsion, which lasted two minutes. He was quiet for a minute or so and then repeated the convulsion. This occurred several times; then he quietly fell asleep." Neurological examination, skull x-rays, and electroencephalograms when awake and asleep were normal.

With amobarbitol sodium, the patient demonstrated complete recall of his feelings and detailed events for the entire period of his spells. In regard to the above-witnessed spell, he was sitting beside a buddy's bed thinking about going to a movie. He remembered that his grandfather had not liked an actor in the movie and then was thinking about his grandfather's terminal illness. He noted a headache; his vision blurred; he began to sway back and forth, felt unable to breathe because of choking in his throat, noted pounding of his heart, and fell to his left onto the bed, face down. He recalled that other soldiers in the room came to his bed, turned him over, suggested calling the medical officer, and tried to hold his mouth open. (His jaws were clenched tightly.) He recalled that he then stiffened his legs and arms and turned from side to side. He recalled: "I didn't want them to hold me." While describing this "seizure" and others, he frequently referred to his grandfather, the latter's terminal illness, and his death a few months before the patient's first spell. He had been close to his grandfather, had cared for him during his terminal illness, and stated, "He died in my arms—I believe if I'd been a little quicker I might have saved his life." While discussing his grandfather, he became tense, began to hyperventilate, then held his breath, threw his head back, arched his back, stiffened his arms and legs, and became cyanotic. Then he began to writhe from side to side. At this point he was slapped on the cheek, told to stop, and asked: "What did you just do?" "I choked up in my throat and couldn't breathe." "Like your grandfather did?" "Yes—he seemed to have something in his throat, choking him." "What else did you do?" "My arms and legs got tight, and I stiffened out all over." "Like grandfather?" "Yes." "Then what did grandfather do?" "He relaxed and was dead." "What do you do?" "I just go limp." "Do you know what you do during your spells?" "Yes—just like grandfather did when he died."

Case 4.—A 19-year-old airman was referred from another hospital, where he had been admitted after an episode in the guardhouse, which was described by bystanders as "convulsions, where the arms and legs are jerking, the patient's eyes are rolled back into his head, and he is trying to bite his tongue." He had sustained a 3-in. scalp laceration "when he fell while having a seizure." The history from the patient indicated that his first spell had occurred soon after entering military service, two years previously, and that he had had about 20 or 30 spells, which had occurred after he

had been thinking about his mother or something that had happened in the past. He would then "get all built up inside," become dizzy, and pass out. He did not know what happened to him after passing out, and upon regaining consciousness he felt tired, confused, and sleepy. For three weeks prior to the last spell he had taken 3 capsules of diphenylhydantion (Dilantin) daily. Neurological examination, skull x-rays, and electroencephalograms when awake and asleep were normal.

With the use of amobarbital sodium, the patient demonstrated complete recall for details of the periods of his spells. In regard to the last one, he recalled that he had returned to the guardhouse from work detail, was thinking about his mother, was disturbed because he had not received any letters from her, and felt that everyone hated him. He began to feel "sick at the stomach" and shortly thereafter requested to go on emergency sick call. At first the request was denied, and, as he shaved, he "became madder and madder." Finally he was told that he would be taken to sick call, and he became so angry that he began to tremble. As he walked to the door of the cell block, he was again ridiculed. He became so angry that he suddenly "flew apart," fell to the floor, striking his head on a bed, and began to kick and swing his arms. (While relating this episode, he demonstrated very realistically this wild, thrashing, kicking, swinging behavior, until he was slapped on the cheek and told to stop.) He recalled being held down, that one guard still maintained that he was "putting this on," and details of the entire period of so-called unconsciousness. He related similar feelings and a similar spell that had occurred at the age of 7 years, after he had been ridiculed by a rival "from the better part of town." He remembered walking to the river by himself and finally becoming so "mad" that he fell to the ground, kicked, fought, and beat his head against the ground. He also recalled similar feelings and behavior at the age of 3 years. A baby sitter had given his sister ginger ale and potato chips but had not given him any because he was "bad." He felt that he was unloved, that everyone hated him, and that he hated everyone else. He went to his room, fell to the floor, kicked, cried, pounded the floor with his fists, and beat his head against the floor.

CASE 5.—A 19-year-old soldier with over two years of military service was transferred from another hospital with a diagnosis of grand mal epilepsy. His first spell had occurred a few days after he had entered military service; he had had a total of 12 spells. The spells were preceded by lightheadedness, sweating, and feeling hot, followed by loss of consciousness for several minutes. Witnesses, including his wife, had told him that he became stiff, shook, and stopped breathing during his spells. He had bitten his tongue, with resulting "bleeding purple spots" on his tongue. During one spell he had allegedly fallen from a second-story ledge. He had been hospitalized at least three times previously for this problem and had been taking diphenylhydantoin and phenobarbital, but had continued to have spells. Neurological examination, skull x-rays, and spinal fluid examination were normal. An electroencephalogram was abnormal because of two paroxysmal nonfocal bursts of 5-per-second high-voltage activity during the waking state.

With amobarbital sodium, the patient recalled that his first episode of loss of consciousness had occurred two years before entering military service, after he had become very hot while exercising and had run into a cool theater. The episode was transient and apparently was not associated with any convulsive phenomena. A friend who had an epileptic brother told him that he might be an epileptic and then described his brother's spells of passing out, tongue biting, jerking, respiratory distress, and rolling around. Although the patient had demonstrated none of these phenomena, he was convinced that he would become an epileptic. On the fourth day of military service he told his sergeant that he had epilepsy and described what his spells would be like. On the fifth day of military service, while losing his money in a crap game, he had his first "epileptic fit." His head felt big; the world and he seemed to be coming to an end; he felt that he had to get away; he felt dizzy, perspired excessively, and felt that he was choking. He then fell to the floor face down with his hands stiffly at his sides. He grabbed the leg of a bunk and then began to roll back and forth on the floor, "breathing hard" and crying; "Mother, Mother (because Mother always stayed with me when I was sick)." He recalled that the sergeant told everyone that he was an epileptic and called for an ambulance. His lips and legs felt numb; he stopped rolling; the sergeant put a spoon in his mouth. Soon two medics came, placed him on a litter, carried him down the stairs "head first to a brown ambulance with a red cross on it," and took him to the hospital. There was no amnesia for any part of the episode. Another spell occurred one night in the barracks, while the patient was losing at a card game. He felt "far away," dizzy, and as though he was choking. He went to a window, opened it, and stepped out onto the second-floor ledge. He walked around the ledge but still felt dizzy and that he was choking. He walked back to the window, saw the men still playing cards, and wondered why they had not come to help him. He then felt that he would like to murder someone, felt that some force was making him fall, and then jumped to the ground below, landing on his feet, with his legs collapsing under him. He then rolled around on the ground and bit his tongue,

"just like epileptics do." A crowd gathered, and after a few minutes he was taken to a hospital and examined. He indicated that all his "epileptic fits" were the same.

CASE 6.—A 22-year-old soldier was hospitalized because of black-out spells. His first spell had occurred at the age of 16; he had had about six spells before entering military service and had had about two dozen spells and three previous hospitalizations during his 10 months of military service. He described his spells thus: "My heart pounds like I'm scared; a funny feeling runs up my back to my head; it feels like it hits something, and I pass out." He had remained unconscious for 15 to 90 minutes and had been told that he "hit the floor, lay there for a short time, and then started jerking all over." After a seizure he awoke with a headache and feeling "foggy," dizzy, and nervous. His grandmother had epilepsy. Neurological examination, x-rays of the skull, and the electroencephalogram were normal.

With the use of amobarbital sodium, the patient recalled in detail the entire period of his last "seizure." The sergeant had awakened the men in the barracks just after midnight to clean the latrine. The patient was angry, felt tired, and sat down on the floor in the corner of the latrine. He began to feel dizzy; his head began to ache; the peculiar feeling ran up his back, and he "passed out." Two other soldiers immediately ran over to him, and one said, "Something is wrong with this man." They put his arms around their necks and dragged him outside. He recalled that he then began to jerk his arms and legs and had difficulty in breathing. He recalled: "It took six men to get me into the ambulance." Then, during the interview, it was suggested to the patient that he was noting a headache, was feeling dizzy, and that he was going to have another spell. Soon he began to hyperventilate, arched his back, and began to jerk his arms and legs in a synchronous, slightly irregular manner; however, he continued to hyperventilate. This continued for about one minute and was followed by violent flinging of his arms and legs, so that it became necessary to summon three corpsmen to subdue him. With more suggestion, he became calm and stated that this was exactly like his other spells. He recalled that the same feelings and behavior had repeatedly occurred in response to feelings toward various people similar to the feelings he had had toward the sergeant. He was then asked to demonstrate how his grandmother jerks during her seizures, and he repeated exactly the same behavior as described above.

Comment

The use of amobarbital sodium in 60 problem cases enabled me to establish a diagnosis of psychogenic-seizure-like spells rather than genuine convulsive seizures in 36 cases in spite of the fact that the history, accounts of witnessed spells, electroencephalograms, or a family history of epilepsy suggested the possibility or likelihood of generalized seizures.

Eleven of these patients had abnormal electroencephalograms. It is not surprising that some patients with psychogenic spells have abnormal electroencephalograms, since 15% of the population have abnormal electroencephalograms[2] and only 0.5% of the population have convulsive disorders.[3]

A statement by a nurse or physician (particularly if the nurse or physician does not deal with seizure problems frequently) that a patient had a grand mal seizure cannot always be accepted as fact. In three cases psychogenic spells had been witnessed and described as grand mal seizures by a physician; in four cases nurses had observed psychogenic spells and mistakenly called them grand mal seizures. In one case the electroencephalogram was abnormal, and spells were observed and described by both a nurse and a physician as grand mal seizures; yet with the use of amobarbital sodium (after 13 months of hospitalization, pneumoencephalography, and arteriography), it became evident that the spells were not genuine convulsive seizures.

A family history of epilepsy in a patient who has spells does not necessarily indicate that the spells are epileptic seizures. In eight of these cases with psychogenic spells there was a family history of epilepsy. Two such patients gave the history that siblings had been in institutions for many years because of epilepsy.

Associated injury does not preclude the possibility that a spell is psychogenic. One patient during a psychogenic spell sustained a scalp laceration; one burned his hand; one had bitten his lips, and three gave a history of tongue biting. In one case the healing laceration had been noted by an examining physician; yet with amobarbital the patient recalled biting his tongue during the strug-

gle that ensued when someone grabbed his tongue.

A by-product of the use of amobarbital sodium in these problems is the insight gained by the physician, and occasionally by the patient, in regard to how some of these psychogenic spells come about. In some cases the behavior demonstrated during the spell was identical with the patient's concept of dying. Some patients exhibited phenomena that had been suggested by seizures of a friend or relative. In others the spells represented nothing more than temper-tantrum patterns dating back to early childhood.

Summary

The demonstration of recall with the use of amobarbital (Amytal) sodium is a useful tool in the differential diagnosis of generalized convulsive seizures and psychogenic spells.

Six typical cases in which recall with amobarbital sodium was helpful are presented.

Abnormal electroencephalograms, descriptions as a grand mal seizure by trained medical witnesses, family history of epilepsy, or self-injury during a spell does not necessarily indicate that a generalized convulsive seizure occurred.

Psychogenic spells may represent childhood temper tantrums, the patient's concept of dying, or the result of suggestion by seizures of a relative or friend.

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Withdrawal Convulsions in Dogs Following Chronic Meprobamate Intoxication

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Clinical evidence is accumulating that abrupt withdrawal of meprobamate (Miltown, Equanil) from patients who have been ingesting large amounts of this agent may be followed by major convulsions. Lemere[1] reported the case of a patient who had ingested 6.4 gm. of meprobamate daily for one month and had a convulsion 10 hours after discontinuation of the drug. Barsa and Kline[2] noted a single convulsion in 6 of 25 schizophrenic patients following withdrawal of meprobamate (2.4 gm. daily for nine months). Tucker and Wilensky[3] reported one grand mal seizure, following discontinuation of the drug, in 2 of 32 psychotic patients who had received 1.6 gm. of meprobamate, increasing to 4.8 gm., daily for three months.

Two cases of this sort have also been observed at the U. S. Public Health Service Hospital, Lexington, Ky.[4] One patient, who had been taking 4.0 gm. of meprobamate daily for about three months, had a grand mal convulsion 34 hours after stopping the drug. Another patient, who received 3200 mg. of meprobamate daily for approximately four months, had definite EEG abnormalities, which were first recorded 24 hours following abrupt withdrawal of the drug, although a convulsion did not occur. Paroxysmal mixed fast and slow EEG activity, resembling that seen during barbiturate withdrawal, was observed between the 24th and the 77th hour of abstinence.

Although these data suggest strongly that meprobamate can produce physical dependence if administered in large enough amounts over a sufficiently long period, the possibility has to be considered that the sporadic occurrence of major seizures in the course of meprobamate withdrawal is related to factors other than, or in addition to, the pharmacological properties of the drug. Ideally, this possibility should be ruled out by a carefully controlled study on "normal" human subjects; but, because of the risks involved, the dog was selected instead, since this species has proved reliable for the purpose of predicting the physical dependence-producing properties of a number of drugs, including opiates and barbiturates.[5,6] In the present report data are presented which show that chronic intoxication with large doses of meprobamate produces physical dependence in dogs.

Methods

Five dogs, weighing between 8.6 and 13.4 kg., were given 1.6 gm. of meprobamate orally at 9-10 a. m. and 3-4 p. m. daily. The total daily dose was increased to 4.8 and then to 5.2 gm. during the subsequent 75 to 130 days. At that time a dose was added at midnight. The total duration of intoxication varied from 124 to 188 days. The final total daily dose of meprobamate ranged between 8.0 and 8.8 gm. Withdrawal was abrupt, and the dogs were observed continuously until death occurred or abstinence signs subsided.

Results

A. Intoxication.—Sleep and/or ataxia (staggering, broad-based gait) was often observed after administration of mepro-

Previously reported in part.[4]

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Meprobamate was supplied by the Wyeth Institute for Medical Research, and the Wallace Laboratories.

From the Department of Health, Education, and Welfare, U. S. Public Health Service, National Institute of Mental Health, Addiction Research Center.

Chronic Meprobamate Intoxication: Dose Schedules and Abstinence Phenomena

	Dog 2	Dog 3	Dog 4	Dog 5
Total days of intoxication	124	164	178	188
Daily dose at end of experiment, mg./kg.	814	656	656	709
Total number of withdrawal convulsions	1 (induced)	3	5	5
Hours of abstinence before convulsions	37	25¼	25½	20¾
Final outcome	Recovery	Death at 26 hr.	Death at 28½ hr.	Death at 20½ hr.

bamate. Prior to addition of the midnight dose, two dogs had convulsions 16 to 18 hours after the last preceding dose of meprobamate. One dog had a convulsion on the 56th day of intoxication while receiving 2400 mg. of meprobamate twice daily. This animal died on the 65th day of intoxication. Convulsions were not observed after the third dose was added. Otherwise, the dogs ate well, remained ambulatory, and maintained their usual physical appearance throughout the period of intoxication.

B. Withdrawal.—The abstinence syndrome was sufficiently stereotyped in Dogs 3, 4, and 5 to permit a composite description. Details regarding each animal are shown in the accompanying Table.

The earliest withdrawal signs appeared 12 to 16 hours after the final dose of the drug. Visible tremulousness, excessive startle response to sudden noise, and an increased frequency of "chop licking" were noted first. Retching and/or vomiting occurred in three of the animals. The dogs became markedly restless, paced at short intervals, and would not remain lying or sitting for more than a brief interval. Unusual behavior, such as staring at the interior of the cage instead of responding to external stimuli, was also noted. Episodic movements of the head were observed shortly before or between convulsions. The head would be drawn back with the nose pointed upward. Although difficult to interpret, this motor pattern resembled tonic retrocollic spasm.

Episodes of violent activity developed just prior to or between convulsions. Some of these movements, although difficult to describe, could well be termed "extrapyramidal." Flinging limb movements or exaggerations and distortions of walking motions appeared to cause the dogs to fall intermittently. Hopping movements of the hindlimbs and circling behavior were also observed. The convulsions sometimes began with a torsion movement of the head and body. Some of the animals appeared to be doubled into a somersault at the beginning of a major seizure.

Major convulsions occurred in the midst of such behavior 20 to 26 hours after discontinuation of meprobamate. Some seizures were more tonic than clonic. In general, the convulsions recurred within a few minutes, until three to five seizures were terminated by death in the three dogs that received the drug for 164 to 188 days. Terminal rectal temperatures were 39.4 and 40.5 C in Dogs 4 and 5, respectively.

In contrast to repeated convulsions terminated by death, Dog 2 (intoxicated 124 days) had only one convulsion and survived withdrawal. Although the other symptoms of abstinence were "spontaneous," the convulsion which occurred at 37 hours of withdrawal was induced by an attempt to remove the dog from its cage to measure rectal temperature. It was evident that attempts to handle this animal during withdrawal precipitated hyperactivity and increased trembling.

Comment

The uniformity and severity of the withdrawal manifestations observed in this study show unequivocally that chronic administration of large doses of meprobamate produces physical dependence in dogs. The relevance of these experiments to addiction to meprobamate in humans is obvious from the clinical reports referred to above. It is also known that barbital sodium creates physical dependence in dogs resembling that seen in man.[6] It seems

likely that the dog is a good animal for testing the addictive properties of the compounds appearing under the terms tranquilizer, ataraxic, phrenotropic, psychotropic, central relaxant, etc., prior to their release for use in patients.

It is often implied that studies on chronic drug intoxications in animals are not relevant to man because of the large doses of drugs used in such animal investigations. This objection cannot be sustained, since, even in man, the demonstration of gross evidence of physical dependence on drugs generally requires administration of the agent in question for long periods of time, at frequent (daily or several times daily) intervals, and in progressively increasing doses, far in excess of "therapeutic" ones. This is especially true in the case of barbiturates or alcohol,[7,8] and the few clinical reports that are available indicate that such are also the conditions that are requisite for the development of physical dependence on meprobamate. Thus, Phillips et al.[9] reported the case of a patient who had been taking more meprobamate than prescribed (14 tablets, or 5600 mg., daily) and who developed abstinence phenomena when the dose level was unwittingly reduced during hospitalization for another reason. A similar instance has already been cited[1] wherein the patient was taking 6400 mg. (16 tablets) daily. Another objection to the use of the dog for testing the addictive properties of new drugs is the implication that this animal is more susceptible to abstinence convulsions than man. The reverse may well be true, since Fraser and Isbell[6] did not consistently observe convulsions following withdrawal of pentobarbital or secobarbital from chronically intoxicated dogs, whereas chronically intoxicated men commonly develop abstinence convulsions and/or delirium after abrupt discontinuation of these drugs.[7]

In addition to physical dependence, the development of tolerance to meprobamate seems very likely. Swinyard et al.[10] found that mice developed tolerance to the elevation of electroshock seizure threshold produced by meprobamate. Lemere reported that nine patients had to take increasing amounts of meprobamate to obtain the initial degree of effect.

Since meprobamate possesses addiction liability, it should be dispensed on prescription only. Physicians who prescribe the drug should observe the following precautions: (1) Meprobamate should be used cautiously in persons who are, or who have been, addicted to alcohol, barbiturates, or opiates; (2) patients receiving the drug should be supervised closely in order to prevent an increased consumption of the drug; (3) meprobamate should be withdrawn slowly rather than abruptly from patients who have been ingesting the drug chronically.

Summary and Conclusion

Meprobamate was administered in a high dosage for 124 to 188 days to four dogs. Abrupt withdrawal of the drug was followed by repeated convulsions and death in three dogs and in an induced convulsion in a fourth dog.

Meprobamate possesses addiction liabilities and should be prescribed with the same precautions used with barbiturates.

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Cinephotomicrography of the Pial Circulation

A Study of Factors Influencing Vascular Caliber; Preliminary Report

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Direct observation of the pial vessels has been carried out for over 100 years.* A window was used by Ravina[20] in 1811. He inserted a short cylinder of wood into a trephine hole in a dog's skull. The top of the cylinder was closed by a watch glass cemented in situ. Donders,[6] in 1859, devised an airtight window and made the observation that when the nose and mouth of an animal were obstructed for as short a time as 10 seconds, dilatation of many small vessels became evident. Many other experimentalists used this method of study of the pial circulation. Thus, skull windows as a means of investigation of brain circulation were carried out by Berlin,[2] in 1851; Kussmaul and Tenner,[15] in 1857; Leiden,[17] in 1866; Riegel and Jolly,[21] in 1871; Elder,[8] in 1897; Lewin,[18] in 1920, and Lee,[15] in 1925. The microscopic studies of Forbes[10] and others through a glass window, beginning in 1928 and extending through the ensuing 12 years, have been the basis for much of our present-day knowledge of the pial circulation. Forbes' window consists of a cover glass fitted into a cylinder, which can be screwed into the skull. Two openings in the cylinder into which 17-gauge needles can be fitted complete the instrument. Through these needles saline and other solutions can be injected to wash the surface of the brain and permit no bubbles of air. Forbes and Cobb,[11] in 1938, suggested that a neural control of the cerebral circulation exists, that the blood pressure and chemical agents, such as CO_2, play a major part, that constrictor nerves are present and are about one-tenth as effective in the pial circulation as in the skin, that vasoconstrictor nerves are distributed unequally in different parts of the brain, and that vasodilator nerves exist. They stated: "Capillaries, at least in the pia, appear always open, the arterioles do not change in caliber appreciably and the flow is remarkable for its steadiness."

We have used the continuous cinephotomicrographic method of recording the pial circulation under different experimental conditions. The vessels are photographed at the rate of 16 frames per second before, during, and after an experiment, and each frame of the record is studied separately. In this respect the cinephotomicrographic record may be compared with serial-section studies of brain tissue. Certain physiological changes that may occur during the course of an experimental investigation can be meticulously evaluated by this technique.

The measurements of the vessels were carried out by studying the individual movie frames under a low-powered microscope with the help of a micrometer placed in apposition to the emulsion of the film and, in turn, the lines of the etched side of the micrometer in apposition to the film. For the purpose of illustrations and figures, the individual movie frames were enlarged to exactly the same size (approximately, a little over 10 times) when photographs of the enlarged image were taken. Camera-lucida projections were also used. Of course, the records also were run in the form of a movie, so as to note the exact

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Neurosurgical Service, Wayne State University School of Medicine and the Grace and Detroit Memorial Hospitals.

* Extensive bibliography on this subject may be found in the papers of Forbes and Wolff[12] and Stavraky.[23]

dynamics of the changes. The magnification on the movie frames was about 4.2 times. However, resolution on the film was excellent, particularly as concerns the caliber of the vessels. From the standpoint of the caliber of the vessels, 40μ to 150μ diameter, it is felt that our records are valid under the experimental conditions described for the monkey. The low-powered-microscopic method of studying the original films with a micrometer next to the emulsion side is quite accurate.

Our observations are based on experiments made upon 182 rhesus monkeys and a few cats and dogs. Results of electrical stimulation of the upper thoracic and cervical sympathetics, the vagus, and the 5th, 6th, 7th, 8th, 9th, 10th, and 11th cranial nerves, and the effects of oxygen and carbon dioxide and of emboli (fat, pumice, air, iophendylate [Pantopaque], etc.) will be analyzed. The effects of stimulation of the pial vessels by faradic and sine wave-currents will be shown. Injection of material into the cerebral circulation was carried out via the carotid artery on the side of the study. In some experiments injections were made into the femoral artery or vein.

The illustrations are photographs of individual frames. An outline of the vessel in question is superimposed. The magnification in the movie frames is $\times$4.2; in the photographs shown, $\times$40.

During the experiments, the vessels were observed at magnifications of $\times$40 and $\times$70.

Experimental Results

1. *Normal Anatomy of Vessels Studied.* The size of the vessels studied ranged from about 30μ to about 300μ. However, attention was focused on vessels between 40μ and 150μ. Smaller vessels were just visible, and their detailed study is being carried out at the present time.

The arteries and arterioles were characterized by their pulsations, and with normal oxygen intake their color was a more brilliant red than that of the associated veins. When the blood pressure was normal and the intracranial pressure was not raised, movements of the blood stream in the arteries were so rapid that the details of the blood cells or their aggregates could not be seen. The appearance was that of a homogeneous mass which expands and elongates with each cardiac impulse. The direction of flow, as one might expect, was from the vessels of the greater diameter to the branches, and all the branches seemed equally filled at all times. The observations made by Jeffords and Knisely [14] and associates that the arteries are in the shape of a truncated cone are supported by a study of our material. The diameter of the vessel becomes smaller distally.

In the rhesus monkey frequent arterioarterial shunts were seen. In arterioarterial shunts the above observations did not hold. That is, the rate of flow in the limb of the shunts is found to differ so much that the blood cells could be seen in one part, owing to the slow movements, while in the other limb the stream was too rapid to permit such observation. The direction of the flow was also found to change in such a shunt, and at times it was found to reverse itself. A shunt appears to remain functional at all times in the observations made thus far.

The normal veins tend to be larger than the associated arteries and are more abundant. The color of the vein is often near that of the artery, especially in poorly oxygenated animals. Direction of the flow is variable, particularly in the smaller veins. Sometimes the direction of flow is changed several times in a minute in the normal animal. Generally the flow is predominantly from the smaller vessels to the larger. The veins are not visibly expansile, but normally pulsations of the blood column are frequently seen. Where the blood pressure and blood volume are within normal range, the velocity of the cells in the vein is rapid and the particulate nature of the stream is barely detectable. There is a decided tendency to lamination of the components of the stream.

Venous shunts are also seen frequently, and, like the arterioarterial shunts, the di-

rection of the flow of the blood may vary. Unlike the arterial shunts, a portion of the venous shunt may become nonfunctioning or disappear completely from the field, to become filled again a little later.

Particularly in hypotensive animals lamination of the contents of the veins may be seen. The more oxygenated blood may be redder; the less oxygenated blood may be bluer, and these columns may extend down a vessel in juxtaposition without mixing. Many such observations were made in embolism studies.

2. Technical and Physiological Problems.

The problem of heating the cerebral surface was an important one, since heat causes dilation of the vessels. With our carbon-arc light source, the temperature of the surface of the brain will rise 6 to 10 degrees C in two minutes. Tap water at about 20 C and with a flow rate 160 cc. per minute was forced through a coil embedded in the window frame used for the study of the surface of the brain. A layer of water over the window was in contact with the coil. Neither the stagnant nor the moving

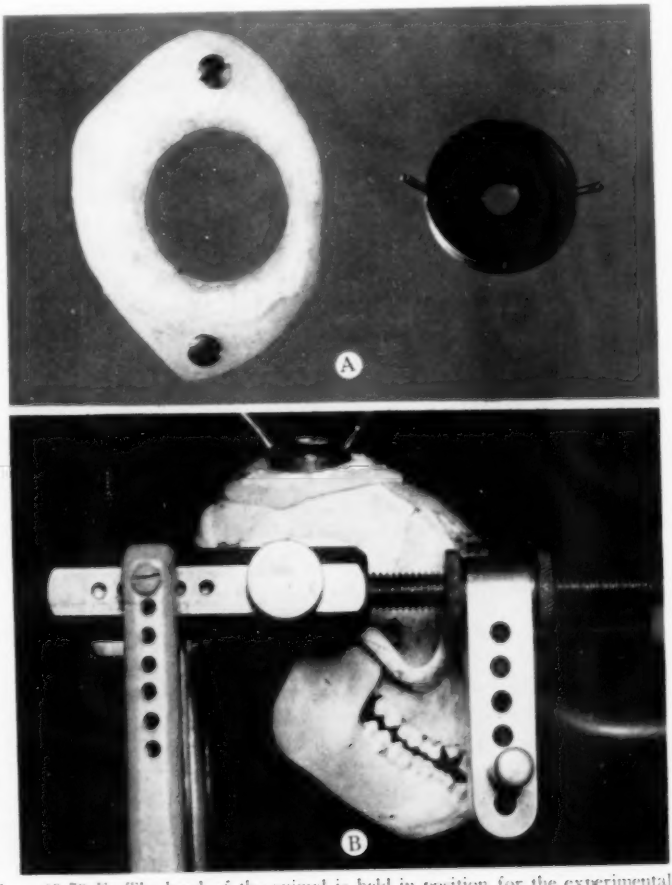


Fig. 1.—Preparation of the rhesus monkey for microscopic study of the blood vessels of the pia. The window, shown in *A*, consists of a flat cylinder, which can be screwed into the protective methylmethacrylate cast, held in place on the surface of the monkey's head with screws. This plastic cast is prepared by pouring methylmethacrylate in its liquid form about the metal cast of the window in position on the unopened dura after a button of bone has been removed with a trephine. When the plastic sets, there are no air bubbles between the window and the skull. The cylinder has a central hole with a cover glass held with adhesive substance to its undersurface. Two metal tubes attached to the window cylinder are for the purpose of passing tap water through the cavity of the cylinder. The tap water does not come in contact with the brain, but it does keep the brain surface at a temperature of about 38 C. With illumination for color cinephotomicrography, heating of the surface of the brain is an important technical source of error. Water passes through the cylinder at a rate of 160 cc. per minute. The temperature of the tap water is about 60-70 F. The head of the animal is held in position for the experimental work. For the sake of simplicity, we have used the skull rather than the intact head. The window was almost always in the right parietal region. A circular piece of dura is excised, with little or no loss of cerebrospinal fluid. The window is adjusted so as not to compress the surface of the brain.

water touched the surface of the brain. Testing of the brain surface under the window with a thermocouple revealed no increase in temperature when the light was on and the water coursed through the coils in the window (Fig. 1). It was found that without a cooling unit 25% to 40% increase in the size of the vessels of 30μ to 150μ diameter was attributable to excessive heat (Fig. 5).

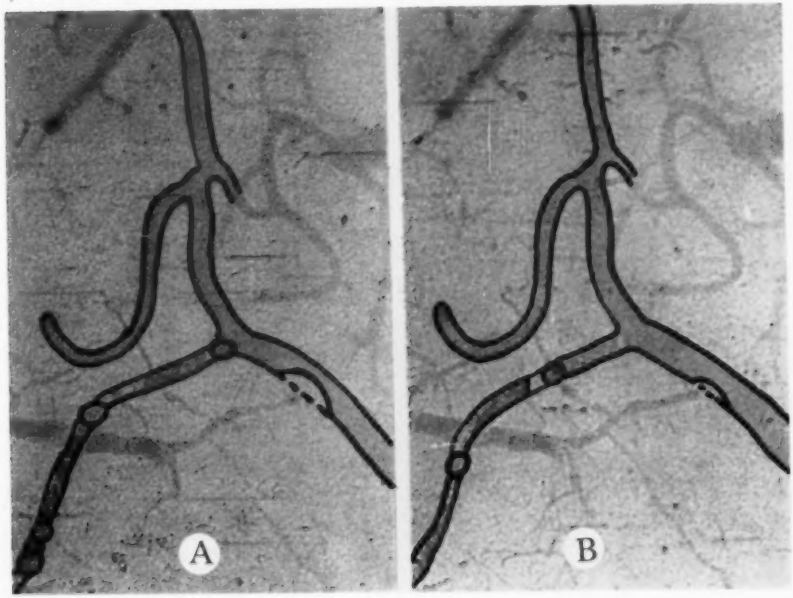
The change in the size of the larger arteries (100μ-300μ) between diastole and systole was studied. At normal blood pressure levels, between systole and diastole, the vessel size changed about 5%.

The blood pressure and respirations were recorded continuously by a Sanborn manometer. Intratracheal intubation was used in all the experiments. The effects of pentobarbital (Nembutal) anesthesia on the rhesus monkey's pia circulation, as well as in other experimental animals, has not been completely evaluated.

The effect of increased intracranial pressure or a tightly fitting window against the bulging brain was evaluated. In a mild degree of bulging of the brain against the window, no change occurred in the diameter of the vessel studied, but there was a difference in the size of the light reflex on the surface of the same vessel (Fig. 6). This gave the impression of the vessel being of larger appearance than normal. Under the circumstance of a severer degree of swelling of the brain against the window, the vessels were found to be dilated because of obstruction at the borders of the window. Under the circumstance of severe increase in pressure, some blanching of the vessels occurred, owing to almost complete obliteration of the vessels.

Fig. 2.—A male rhesus monkey, weighing 10 lb., with the window placed in the right parietal area; blood pressure 130/92; pulse 156; respirations 36. Iophendylate (Pantopaque) emulsion, 0.2 cc., consisting of 3 parts of iophendylate, 2 parts of water, and 1 part of acacia, mixed together at high speed, was injected into the right carotid artery. Three injections were made. The animal lived 3 hours 30 minutes after the first injection. Autopsy revealed much of the injected material in the lungs. Pentobarbital (Nembutal) anesthesia was used; corneal and gag reflexes were intact.

A shows a large nick in the artery, caused by a small, colorless deposit of iophendylate with fibrin. In 12 minutes enough of the fibrin-iophendylate deposit was washed away. The photograph in *B* shows the nick much smaller and the lumen of the vessel much larger.



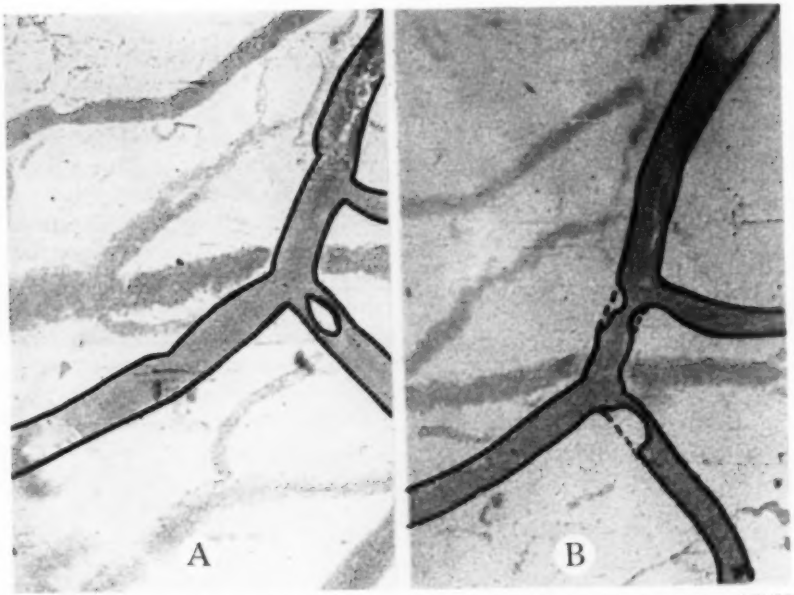


Fig. 3.—Rhesus monkey, weight 10 lb.; pentobarbital anesthesia; blood pressure 142/100; pulse 140; respirations 48. One-tenth cubic centimeter of pumice colored with metallic blue and suspended in saline was injected into the right carotid artery at 1:00 p. m. The immediate effect was a rise in the pulse pressure (142/64), lowering of respirations to about 6 per minute, and a rise in the pulse rate (190), with a paradoxical pulse. Over a period of 20 minutes, the pulse improved, the pulse pressure remained wide, and the respirations increased. *A* shows fibrin deposit about pumice in the vessel, 30 minutes later simulating a nick with partial occlusion of the vessel (*B*). When *B* was photographed, the animal's circulation was poor; the flow in the vessel was stopped except for the back-and-forth movement of the column with each cardiac impulse. The surface of the vessel was irregular, due to aggregation of blood in clumps, with transparent plasma near the periphery. Actual magnification is ×4.2; the photographs shown are about ×40. The effects of injection of pumice were worse than those of iophendylate emulsion or pure oil. Air causes occlusion of vessels more effectively than any of these substances.

3. *Effect of Mechanical Obstruction of Carotid Arteries in the Neck.*—The internal carotid artery was occluded by means of a ligature in a rubber tube so that occlusion could be obtained, maintained, and released without moving the animal. Cinephotomicrographic records were made during both unilateral and bilateral occlusions (Fig. 7).

The most obvious change followed bilateral occlusion. The expansional movements of the arteries stopped completely, and the vessels appeared to relax, tending to straighten out. The particulate matter of the blood stream could be seen, and in some arteries momentary stoppages of the flow occurred. Over a period of several seconds the color of the arteries changed to a dusky-red hue. Then the slow movement in the original direction started again, with pulsating movements of the column of blood but without expansion or lengthening of the vessel. During this period some reduction, followed by increase, in size of the arteries was seen (Fig. 7). Within about two minutes the stream was moving quite rapidly, and the vessels had assumed their previous color. In spite of continued occlusion, there was a resumption of flow of oxygenated red cells, probably from the vertebral arteries. The velocity of the stream tended to become normal again. As long as the occlusion was maintained, no expansile pulsations were noted. These reappeared as soon as the occlusion was discontinued. The changes noted in the arteries following ipsilateral occlusion of the

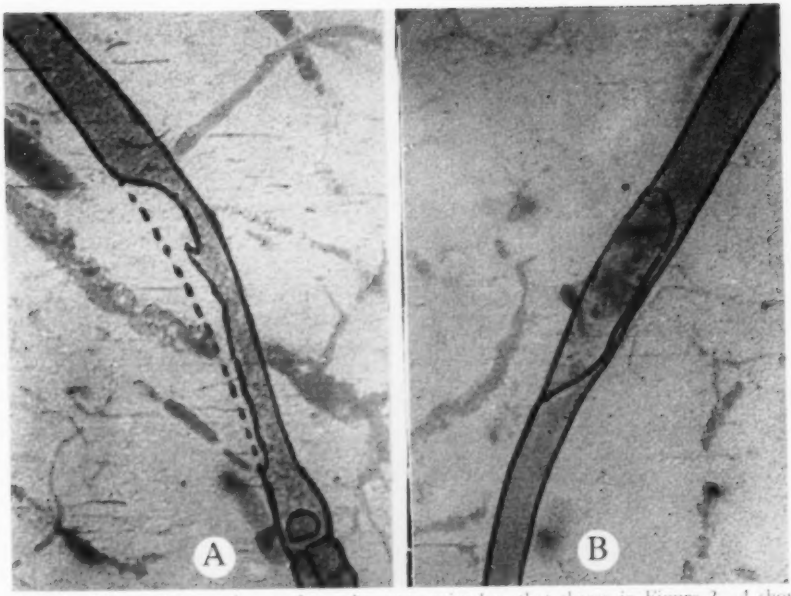
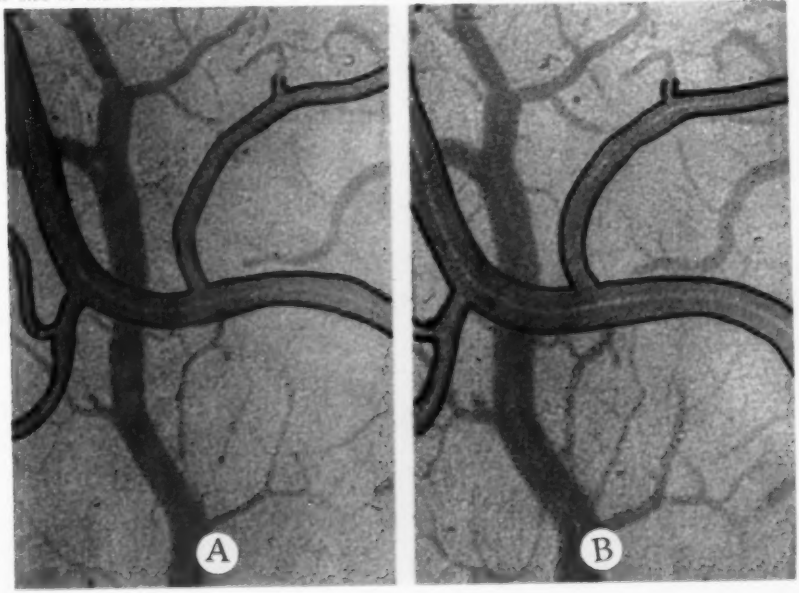


Fig. 4.—These photographs are from the same animal as that shown in Figure 2. *A* shows the narrowing of the lumen of the vessel, due to a colorless deposition of fibrin along the vessel wall. The narrowing is distal to the embolus, which may be seen in the outline of the vessel to the right. In *B* is seen the relative dilation of the vessel proximal to the embolus and narrowing of the vessel distal to the obstruction. A small amount of blood can pass by the area of the obstruction. These effects of dilation proximal to the obstruction and narrowing distal to the obstruction are mechanical.

Fig. 5.—Male rhesus monkey; weight 13 lb.; pentobarbital anesthesia. A, arc-light illumination with the surface temperature recorded at 38 C. B shows two minutes of illumination of the surface of the brain without tap-water circulation through the window. A 35% increase in the size of the vessel can be seen.



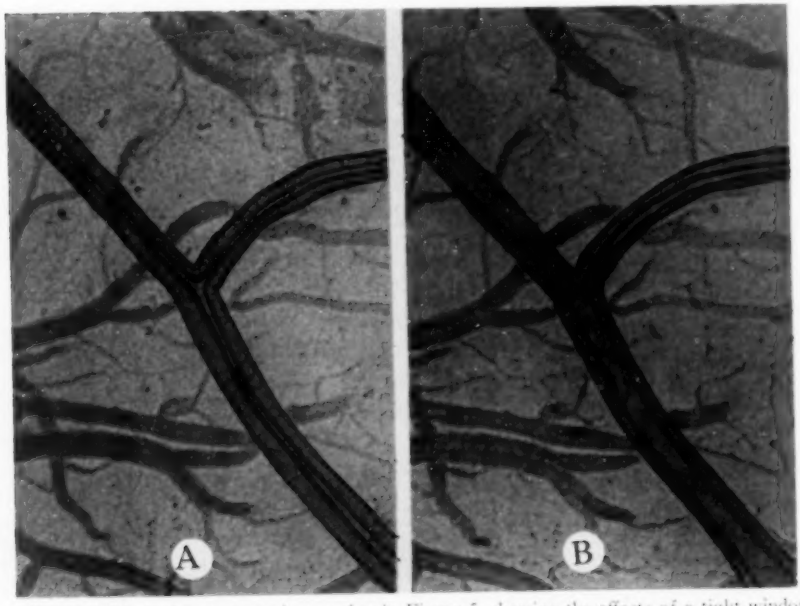


Fig. 6.—This is the same monkey as that in Figure 5, showing the effects of a tight window. (*A*) The window at a normal position; (*B*) flattening of the artery against the window, shown by an increase in the size of the light reflex on the vessel wall. On loosening the window, the light reflex returned to its normal position, and the pulsations of the vessels could be seen. In this instance there is no real increase in the size of the vessel, but with the flattening of the light reflex in *B* an illusional increase in size may be obtained.

internal carotid artery were minimal. There was a decrease in the amplitude of the expansion of the vessel with each cardiac impulse. Slowing of the stream was barely detectable, and there was no color change with ipsilateral occlusion.

Prominent changes were noted in the veins of comparable size with bilateral occlusion of the internal carotid arteries. The stream of blood cells was seen to stop and its color to become bluish-dusky red; later the stream started to move, even though the occlusion was maintained. The arrest persisted longer, and the resumption to a normal velocity also was delayed. Unlike the artery, the direction of flow in the veins may reverse, and this is seen particularly in the smaller tributaries, which may be flowing toward the heart at one time and then later in an opposite direction. A prominent feature was the manner in which certain venous tributaries temporarily emptied and were obliterated from view. Compared with the flow in the arteries, flow in the veins is resumed with increasing velocity, until after six minutes of maintained bilateral occlusion, the velocity becomes nearly normal. Ipsilateral occlusion of the internal carotid artery produced a more definite effect on the veins than it did on the arteries. However, the change was minimal as compared with that with bilateral occlusion.

During occlusion, vessel size increased in the neighborhood of 10% to 15% at the end of two minutes. Later, with more normal circulation, the arteries returned to the original size (Fig. 7).

4. *Studies in Embolism and Effects on the Circulation.*—Air, oil, fat particles, pumice, emulsions of oil with particles of certain size, etc., were studied in both acute and chronic preparations.

When 0.1 cc. of air was injected into the carotid artery, the air entered the larger vessels of the pia and stopped at the junc-

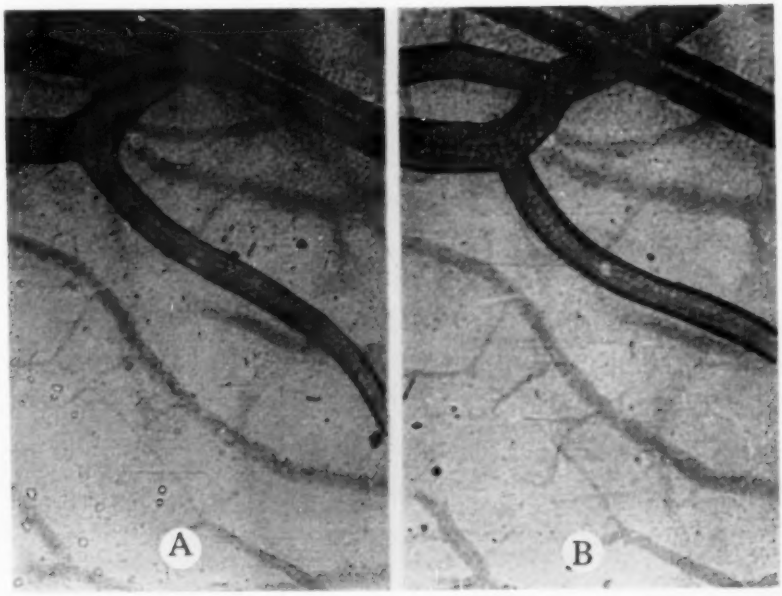
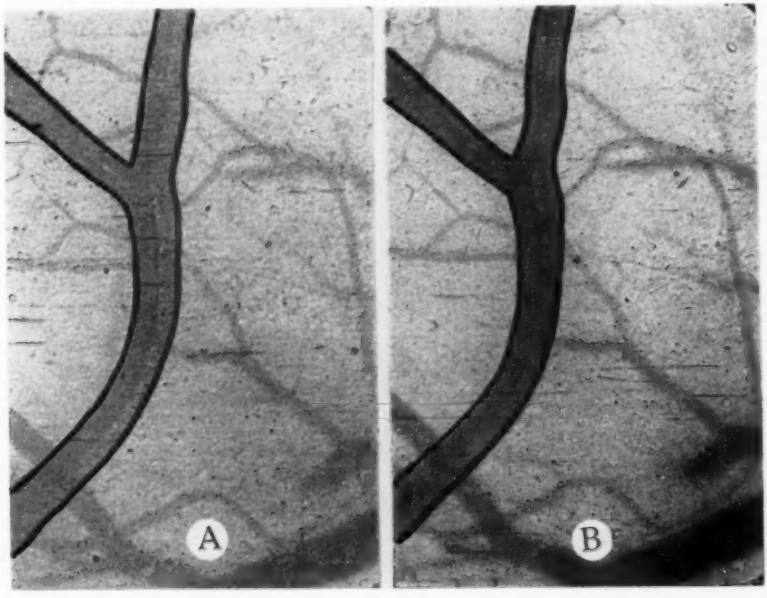


Fig. 7.—*A* shows the state of the vessels before bilateral carotid occlusion. *B* shows 10% increase in the size of the vessel after two minutes of occlusion. Other changes following bilateral compressive occlusion of the carotids are described in the text.

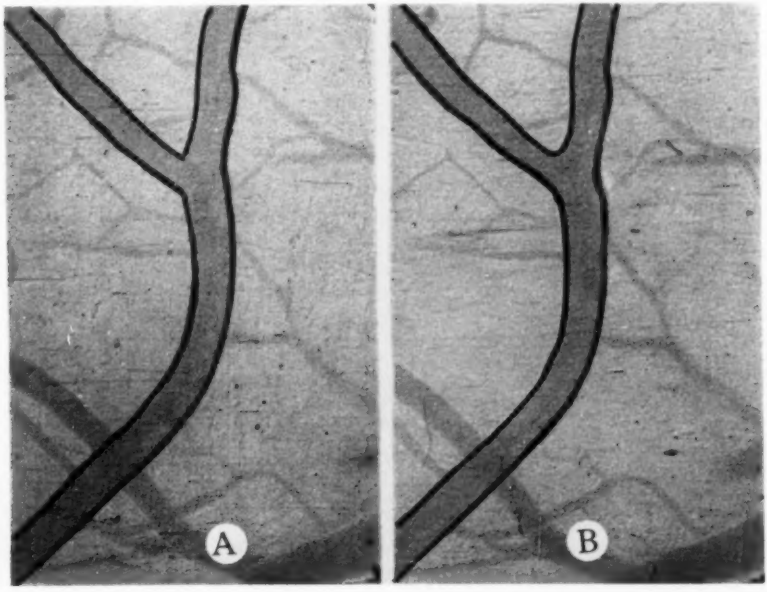
Fig. 8.—Female rhesus monkey, weighing 10½ lb.; pentobarbital anesthesia; blood pressure 80/64; pulse 48; respirations 30. Vagus stimulation after section. The proximal end of the vagus was stimulated with Rhoan stimulator, utilizing interrupted current, 60 cycles, 1 to 10 volts. No significant change in vessel size is noted.



tion of the vessel with smaller branches. In vessels of 50μ diameter or less, there was a tendency for the vessel to become distended around the globule of air. In some of the smaller vessels (about 30μ to 20μ) the globule of air was trapped and was made to proceed forward or in the opposite direction, causing the vessel wall to be several times as large as normal about the air embolus. When the air completely disappeared from the vessel, blood immediately replaced it. It was evident from air embolism studies that the pial vessel walls are transparent, since when air replaces the blood in the lumen, the vessel walls were glass-like, even in vessels of 150μ-500μ.

When 0.1 to 0.3 cc. of oil was injected into the ipsilateral carotid artery, the oil divided into smaller globules, and these smaller particles then passed from the larger vessels into the smaller vessels. Divisions occurred at each branch of the larger vessel. When a complete occlusion of the vessel occurred, the portion of the vessel distal to the occlusion became somewhat smaller, suggesting that the size of the vessel is in part controlled by the distention by the circulating blood (Fig. 4). Some animals were given intracarotid injection of 0.1 to 0.3 cc. of oil and were permitted to live for as long as seven days. Restudy of the surface of the brain revealed evidence neither of the oil nor of any abnormal vascular phenomena. An accumulation of the oil in the lungs was found on postmortem investigation. It is interesting to note that, whereas iophendylate emboli could be followed from the artery into the large veins in the same area of study, with oil particles this was seldom the case. In chronic preparations, the colored oil particles disappeared almost completely, suggesting that these particles of whatever size eventually proceeded on, squeezed through the capillaries, and became collected in the lungs.

Fig. 9.—Records from the animal in Figure 8 with stimulation of the distal portion of the vagus. Stimulation of the distal end of the cut vagus resulted in bradycardia, and some increase in blood pressure at the time of the stimulation, with lowering of the pressure immediately afterward. Deep respirations were followed by rapid respirations and more normal breathing, with return of the normal pulse rate and pulse pressure as the stimulation was stopped. Experiments on the vagus were carried out in 11 monkeys; four to eight stimulations were carried out on each animal.



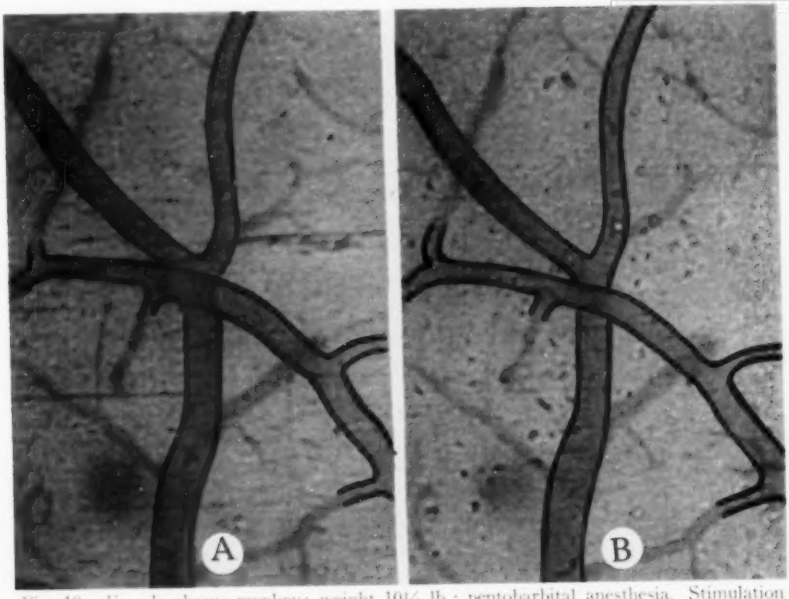
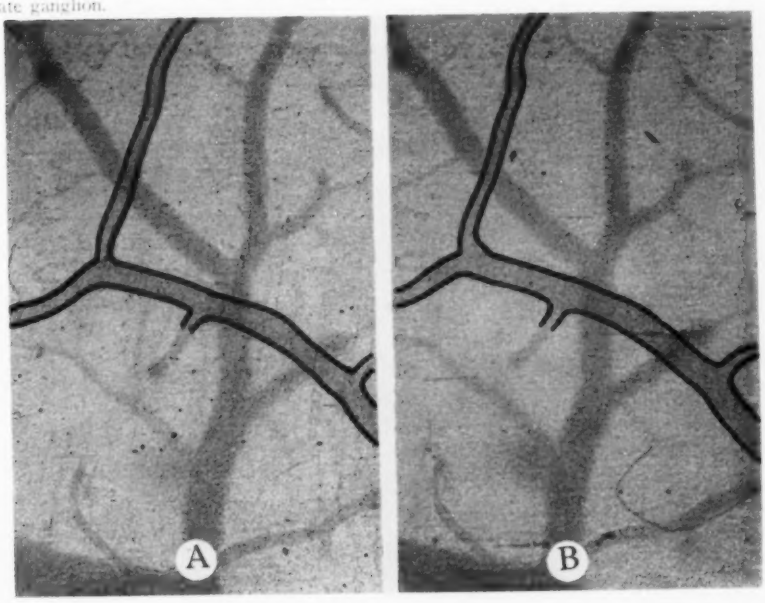


Fig. 10.—Female rhesus monkey; weight 10½ lb.; pentobarbital anesthesia. Stimulation of the vagus nerve resulted in a change in the position of the artery in relation to the vein, due to the vigorous pulsations during the bradycardia, as may be seen by the angle between the artery and the vein which crosses over the artery. An immersion cone, brought close to the surface of the brain, was employed in some of these experiments, with tap water used to keep the surface temperature to normal level.

Fig. 11.—Same animal as in Figure 10. Stimulation of the stellate ganglion resulted in dilation of the pupil in every instance in which it was attempted. This was obtained with 2 volts' stimulation of the neural tissue. These animals did not have any atropine. No change in the vessel size was noted when stimulation was done with low voltages sufficient to produce a dilation of the pupil. *A* is before sympathetic stimulation, and *B*, after stimulation of the stellate ganglion.



Injection of pumice and other solid colored particulate matter resulted in the implantation of some of the material on the lining of the vessels. Under these circumstances, the flow through that vessel was slower, and the portion of the vessel distal to the partial occlusion was definitely smaller than the proximal area.

In these studies the endothelial wall of some of the vessels developed local fibrin aggregates, suggesting constriction of the vessel. However, careful study of the vessel showed that the aggregate collected in the vessel wall was within the confines of the diameter of the vessel seen in the cinemicrophotographic records. In some instances, such aggregates became less evident and disappeared, permitting the vessel to become completely refilled with blood. We did not see evidences of sustained spasm, as described by Villaret and Cachera[25] (Figs. 2 and 3).

5. *Carbon Dioxide and Oxygen Inhalation and Their Effect on the Vascular Size.*—The inhalation of 40%-100% carbon dioxide for one minute resulted in a marked dilation of the pial vessels. The enlargement was from 25% to 40%. In Figure 13, before the use of carbon dioxide, the size of the artery may be seen to the left. To the right, after the use of carbon dioxide for one minute, the size of the vessel increased about 35%. As soon as oxygen was readministered, the vessel size returned to normal. The blood pressure and respirations increase on CO_2 inhalation. There is also some slowing of the pulse.

Inhalation of 100% oxygen resulted in some degree of contraction of the vessels. This, however, was not as evident as the relative distention of the vessels on carbon-dioxide inhalation. A 10% to 15% decrease in the vessel size was found. In some portions of the vasculature there was not any appreciable change in the vessel size on O_2 inhalation. In these experiments the oxygen per cent saturation and the carbon dioxide content of the blood of the animal were not measured at the time of the experiments (Fig. 14).

6. *Stimulation of Vagus, Cervical and Upper Thoracic Sympathetic Chain and Ganglia, and Fifth to Eleventh Cranial Nerves* (Figs. 8, 9, 10).—Stimulation of the vagus by a 1-10-volt, 60-cycle faradic current, unilaterally and bilaterally, was associated with a marked decrease in the pulse rate. The artery pulsations appeared to stop with each diastole, which was prolonged. With systole the vessel appeared to elongate and distend, with an increase in the velocity of the stream. No appreciable change in the size of the vessels was noted after bilateral or unilateral vagus stimulation. The relative blanching of the surface of the brain, which was seen initially, was thought to be due to the bradycardia. When the cut vagus was stimulated peripherally, the same cardiac effects were noted reflected in the cerebral flow (Fig. 9). This flow is reduced, owing to the bradycardia rather than to vasodilation, as suggested by Schmidt.[22] Stimulation of the central portion of the vagus resulted in no changes in the vessel size (Fig. 8). The blood pressure record during vagus stimulation showed an initial increase in the systolic level, with an increase in the pulse pressure with bradycardia. Immediately following the stimulation there were a lowering of the pressure and narrowing of the pulse pressure. The drop in pressure was minor when pre- and poststimulation pressures were compared (from 90-70 mm. Hg).

Stimulation of the sympathetic chain in the neck and the cervical and upper thoracic ganglia by 60-cycle faradic current resulted in no change in the vessel size in the vessels studied (Fig. 11). In these experiments the condition of the pupil was recorded and dilation of the pupil was considered to be an evidence of sympathetic stimulation. Twelve experiments were carried out for this purpose. It was noted that in some of the monkey preparations there were large neural connections between the sympathetic chain and the vagus nerve. This explained the bradycardia in some cases as resulting from overflow of the current to the adjoining vagus.

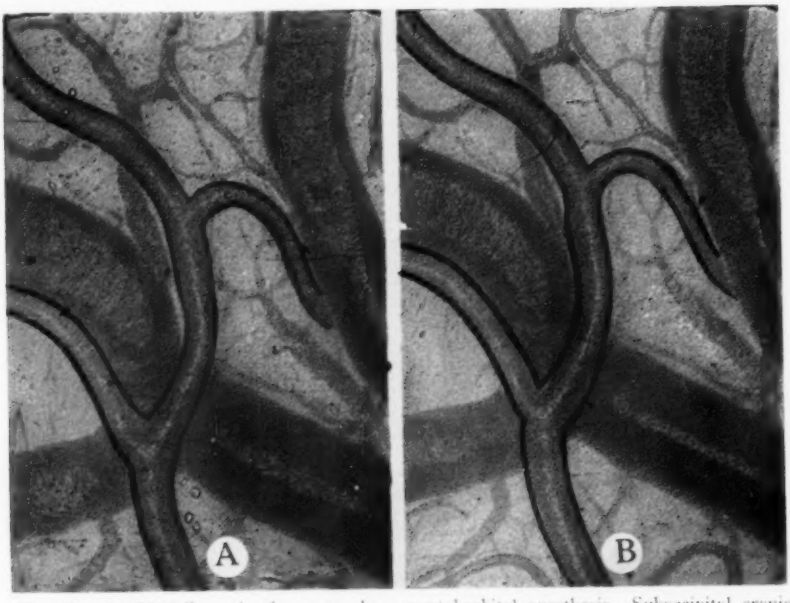


Fig. 12.—An 11½ lb. male rhesus monkey; pentobarbital anesthesia. Suboccipital craniectomy with exposure of the 5th, 6th, 7th, 8th, 9th, 10th, and 11th cranial nerves. The nervus intermedius could be easily separated from the facial nerve in this instance. *A*, before stimulation of the intact facial nerve; *B*, after 90 seconds' stimulation of the intact facial nerve, with no change in the vessel size. The seventh nerve was cut, and the distal end of the cut nerve at the internal meatus was stimulated, with no change. In each instance, tetany of the facial muscles could be obtained with 0.8 volt at 60 cycles from the Rhom stimulator. If more voltage was used, the animal would go into convulsive movements of the body, making photography almost impossible. Stimulation of the 9th, 10th, and 11th cranial nerves caused no change in vessel-wall size. Muscular movements involving the shoulder area were seen with 11th-nerve stimulation. There were no significant alterations in the pulse rate, which was 150, or the blood pressure, which was 120/60. Respirations were 24 and remained fairly even. The illumination source was thought to be 534 watts of arc light cooled with the window-water circulation.

Experiments were performed in which the seventh cranial nerve was carefully exposed as it entered the internal acoustic meatus (Fig. 12). The intact nerve and the peripheral and central stumps after section were stimulated with faradic (1-10-volt, 60-cycle) current. The surface vessels were continuously photographed for as long as 10 minutes after the beginning of the stimulation. In our records no significant change in size of these vessels was obtained. We were unable to confirm the findings of Chorobski and Penfield,[3] who reported dilation of vessels from such stimulation in the monkey. In our hands, stimulation was repeated four to six times in four different animals with no change in the vessel size. With adequate stimulation of the facial nerve, marked contractions of the facial muscles were noted (0.4-volt, 60-cycle faradic current). Frequently, during stimulation, increased lacrimation was noted on the ipsilateral side.

Stimulation of the 5th, 6th, 9th, 10th, and 11th cranial nerves at the cerebellopontine angle did not result in any change in the vascular caliber. In one example the nerve of Wrisberg could be separated from the seventh and eighth cranial nerves. In this instance stimulation of the nerve resulted in no change in the pial vasculature (Fig. 12).

7. Electrical and Mechanical Stimulation of Pial Vessels.—Electrical stimulation of arteries was carried out by bipolar and monopolar means. With the use of a micro-

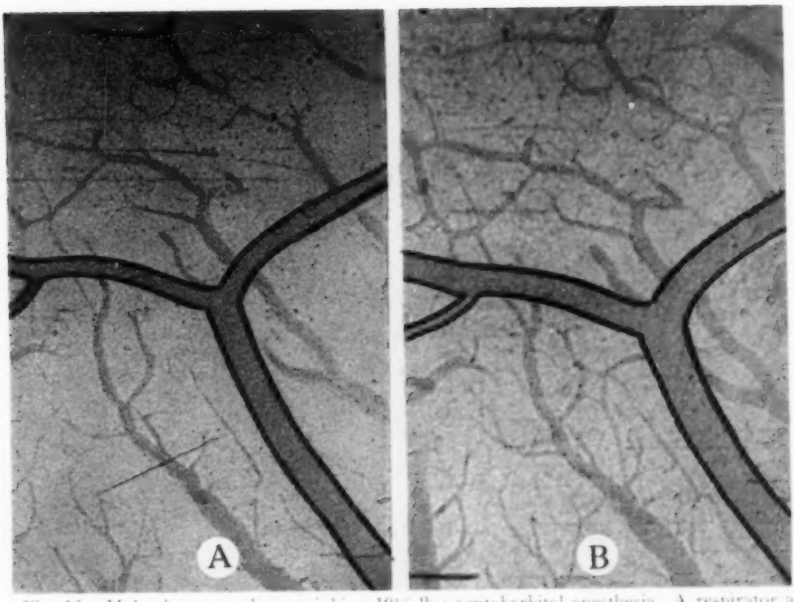
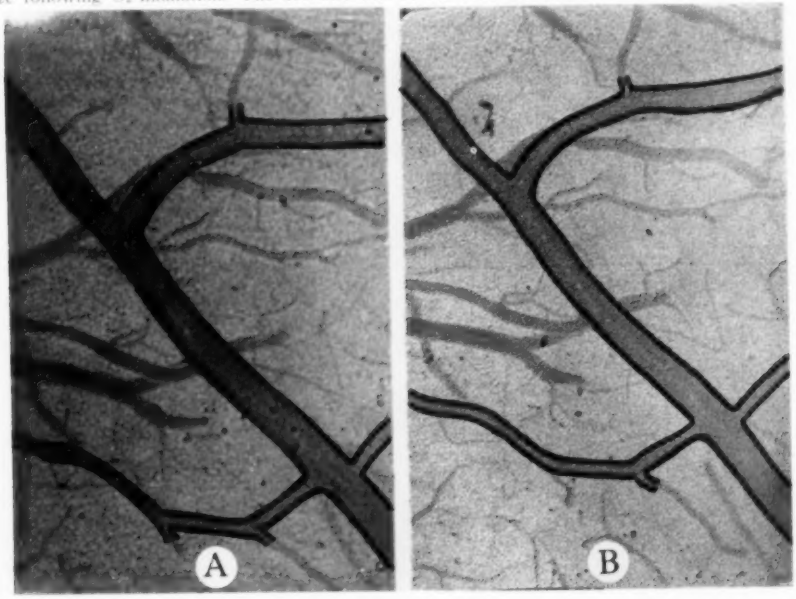


Fig. 13.—Male rhesus monkey, weighing 10½ lb.; pentobarbital anesthesia. A respirator and anesthesia machine were used to deliver various gas mixtures. In this instance, 100% carbon dioxide was used for two minutes. Before CO_2 the blood pressure was 144/84, respirations 25, and pulse 35. After two minutes of CO_2, the blood pressure rose, there was slowing of the pulse, and respirations increased from 25 to about 80 per minute. The animal appeared to be in physical stress. The blood pressure rose to 180/104. *A* shows the vessels before CO_2, and *B* shows the vessels after two minutes of CO_2. An about 35% increase in size of the vessel may be seen. During this experiment there was a tendency for the brain to press against the window. It was felt that the increase in the size of the vessel was mainly due to the CO_2 inhalation rather than an increase in the blood pressure.

Fig. 14.—Female rhesus monkey; weight 10 lb.; pentobarbital anesthesia; blood pressure 160/100; pulse 160; respirations 40. *A* shows appearance of the vessels with the animal in room air; *B* shows appearance after two minutes of 100% O_2. In *B* a 15% to 18% decrease in the size of the vessel may be seen. The majority of animals showed a definite decrease in vessel size following O_2 inhalation. The decrease was of the order of 15%-20%.



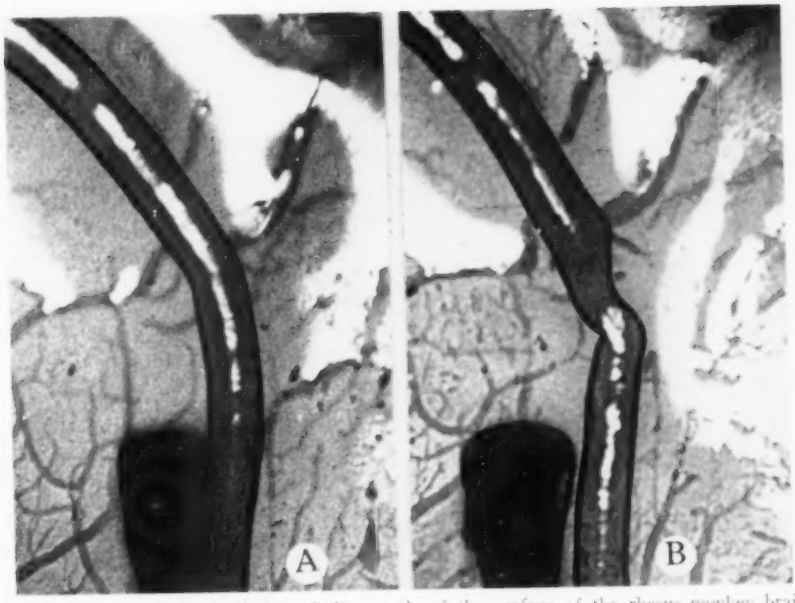


Fig. 15.—Electrical stimulation of the vessels of the surface of the rhesus monkey brain. With a Rhom stimulator a current of 0.1 to 10 volts at 60 cycles was used, with no change in the vessel-wall size. In this instance the electrical coagulation unit was used from a Cameron cauterodyne, causing a shrinking of the vessel wall on one side more than on the other and giving the crooked appearance in *B*. In the rhesus monkey electrical stimulation and mechanical stimulation of the arterial structures did not result in spasms or irregularity of contour, under pentobarbital anesthesia.

manipulator the vessels were contacted, and faradic and 60-cycle sine-wave and sawtooth currents up to 10 volts were applied. It was found that vessels can become obliterated by appropriate current of adequate voltage and amperage, but this was due to electrocoagulation and desiccation, rather than to vasoconstriction. It is comparable to clumping and shortening of the dural lining when this is touched with the electrocoagulation unit in the operating room. When a vessel was made to disappear or shrink, this change was generally permanent. When a portion of the vessel wall was burned, the vessel became deformed, as can be seen in Figure 15. Mechanical irritation of the vessels never caused constriction in these studies of vessels 50μ-150μ in size. When one compressed the vessel sufficiently to interfere with the normal flow of blood, the distal portion of the vessel became somewhat smaller, as has been noted under other experimental conditions (Fig. 15).

Comment

The technical problems involved in obtaining consistent cinemicrophotographic records of the pial circulation on colored film include achieving adequate magnification, light source, control of movements of the brain of the animal, and temperature control.

Since colored film requires more light for proper exposure than does black and white, the quality and quantity of light presented the greatest difficulty. Only reflected light could be used, and this was extremely intense in order to sensitize a film at a plane more than 160 mm. from the objective, a distance necessary to obtain the desired magnification of about $\times$ 4.2. Carbon-arc light, while theoretically too blue for use with Kodachrome Type A film, gave the best results.

The problem of heating of the cerebral surface was overcome by using a water-cooled window. Tap water of about 15-20 C was forced at the rate of 160 cc. per minute through a coil which was embedded in the window structure. The coil is a plastic material, 8 in. (20 cm.) long and 0.5 mm. in diameter; a layer of water over the window is in contact with the coil. Neither stagnant nor moving water touches the tissues. A coil system was also used in the optical glass water jars to control to some extent the heat from the light source. With a carbon-arc light, thermocouple studies have shown rises of 6-10 degrees (C) in two minutes.

The depth of field in which one works at this magnification is less than 1 mm. The long arm of the light axis is between the objective and the focal plane. It follows that even the slightest movement vertically or horizontally will result in gross distortion of the recorded image. Our early efforts revealed that three types of movements have to be avoided. These were the physiological movements of the brain, the movements due to the activity of the animal, and the movements produced by vibration of the camera and the building.

The laboratory vibrations were avoided by designing a heavy camera stand of several hundred pounds' weight. This was then bolted and braced to a cement floor and wall. The camera and objective were made in one piece and bolted to a stand. The vertical movements of the camera necessary to focus are accomplished by a worm-gear device, which moves the camera up or down, 1 in. by 540 turns of the focusing crank. This allows for a more precise adjustment than the standard microscope micrometer. The vibration of the camera produced by its motor is avoided by driving the camera from a separate motor through a V-belt. The necessity for winding the camera is obviated. The whole recording can be controlled by a remote electric switch. The motor is equipped with a variable rheostat and a tachometer, which allows records to be made at a speed ranging from 8 to 64 frames per second. Most of the records used in these particular studies were made at 16 frames per second.

The movements of the animal were prevented by fixation of the head by its bony prominences and meatuses on a specially designed table (Fig. 1). This, in turn, is securely fastened to a table with a micrometer-adjusting device. The table is, in turn, bolted to the floor. A recording of fine movements of the pial field before the camera lens is therefore possible without extrinsic movements.

In order to observe and record at the same time, a beam-splitting device was used. Ten per cent of the light entered the eye and the remaining 90% was used for sensitizing the film by being directed to the focal plane through a 90-degree bend. The observation ocular gave magnifications of $\times 40$-$\times 70$. The objective presently used is a Cine Ektar f/1.4 reversed to correct conjugate aberration. It is mounted directly on the beam-splitter housing. The camera is a Cine Special with provision for use of 200-ft. rolls of film.

Except in a few experiments, all animals were adult rhesus monkeys. The experiments were done with the animals under pentobarbital anesthesia; blood pressure and respirations were recorded. An intratracheal tube was used for a free airway and to control respirations in certain experimental procedures.

The material discussed in the previous pages points to certain physiological and experimental errors. In the larger vessels it was possible to show a slight change in the size of the vessel during a complete cycle of systole and diastole. With records being obtained every thirty-second of a second, such a change is more easily recorded than by observation with the naked eye or the use of occasional photographic records. Blood pressure changes definitely influence vascular size of the pial circulation. This has been noted by many investigators (Ask-Upmark,[1] Fog,[9] and others). A drop

in pressure may result in an initial narrowing of the vessels with an increase in size in the vessels soon afterward.

The problem of heating the surface of the brain from the light source is extremely important, since in our experience as much as 25% to 40% change in the size of the vessels may occur when the surface of the brain is heated (Fig. 5). The effects of anesthesia on the vessel-wall reactivity may also be important. We hope to be able to report soon on studies under local anesthesia in the human.

Many authors have pointed out that in the use of a window, the possibility of increased intracranial pressure causing a bulging of the surface of the brain against the glass window may produce a change in the size of the vessels from the pressure. As stated previously, when the pressure is mild, only the light reflex on the vessel wall changes, giving the impression of a larger size. On measurement the vessel size may be found to be the same (Fig. 6). There may be dilation of the vessels from obstruction. In a very severe degree of bulging of the brain against the window there may be blanching from almost complete obstruction of the vessels. In our hands, no difficulty was encountered in exposing the surface of the brain. No "air bubbles" were noted after the insertion of the window.

In the studies so far recorded it appears that mechanical (cardiac) and chemical (O_2, CO_2) mechanisms are the factors controlling the size of the pial vessels. That these vessels are passively dilatable is unquestioned. That an increased blood pressure may cause a relative enlargement of the vessels, and that a decreased blood pressure may initiate a contraction of the vessels, followed by dilation due to chemical changes, are mechanical results that have been frequently seen (Ask-Upmark,[1] Fog[9]). With such mechanical influence, the possibility exists that chemical mechanisms may also modify the vascular response. For instance, with a drop in blood pressure, it is also possible to have an inadequate oxygen supply and increased CO_2 tension, with consequent dilation of the vessels. The most important means of dilation of vessels was the use of carbon dioxide in these experiments (Fig. 13). A smaller percentage of contraction, when compared with the relative distention due to carbon dioxide, was obtained with the use of oxygen (Fig. 14).

The presence of active vasoconstrictor and vasodilator nerves influencing the condition of the pial vessels could not be proved by these experiments. Stimulation of sympathetic nerves in the monkey, and stimulation of the central stump of the vagus and the facial nerve did not reveal unusual degrees of response above the experimental error involved in technique (Figs. 8-12). Forbes and Wolff,[12] Stavraky,[23] Forbes and Cobb,[11] and Chorobski and Penfield[3] reported constriction of pial arteries on sympathetic stimulation and dilation on stimulation of the facial nerve and the central stump of the vagus. Although the results were not uniform, Forbes and Wolff[12] stated that light anesthesia resulted in more successful experiments.

The question of spasm of vessels of the size studied was evaluated by mechanical and electrical stimulation, as well as in experiments employing emboli. In many instances fibrinous aggregates developed on the inner wall of the vessel, giving rise to a narrowing of the lumen through the area of the aggregation (Figs. 2, 3, and 4). With careful study of these vessels, it was seen that this phenomenon was not related to a spasm but, rather, was a mechanical illusion. It was found that immediately beyond an area of partial obstruction the vessel became smaller as compared with its proximal portion. This has been recorded on several occasions. This change was also thought to be due to a mechanical factor rather than to a so-called spasm (Fig. 4).

Electrical and mechanical stimulation of the vessels resulted in no true spasm. Mechanically touching the vessel by the micromanipulator was never successful in producing changes in the vessel wall in

these experiments. These results differ from those of Villaret and Cachera[25] and Echlin.[7] However, Echlin stated that in the monkey such changes were hardly ever seen, and in this respect the monkey differed from the cat. The use of unipolar stimulation, electrical, and bipolar electrical stimulation resulted in no change in the vessel size. With higher voltages and amperages, vessels could be coagulated, with complete and permanent obliteration of the vessel lumen. Obliteration of the lumen due to shortening and contraction of the vessel wall or partial obliteration and narrowing of the lumen from less complete involvement of the vessel wall is not an example of spasm. Under these circumstances, no spasm has occurred; only a shortening of the fibers, due to the electrocoagulation and desiccation, has taken place (Fig. 15).

Any of the above conclusions may in part be influenced by species characteristics. It is conceivable that some species, particularly the human, may not behave in the same manner in comparable experiments. However, most of the information in textbooks now being applied to the human is based upon experimental data derived from studies upon the cat. Anesthesia also may be an important factor in variability of results.

During the past 50 years many studies have been carried out to show the presence of nerve fibers in the adventitial wall of the pial vessels. The works of Huber,[13] Stöhr,[24] Clark,[4] Penfield,[19] and others have shown the presence of myelinated and unmyelinated fibers in cerebral vessel walls. The question arises as to why these blood vessels are innervated as are blood vessels elsewhere in the body. Even though the finer vessels, according to Stöhr[24] and Penfield,[19] may not possess nerve fibers, the larger vessels have actually an innervation comparable to that of systemic blood vessels. In phylogeny, the fact that a structure is discernible does not necessarily indicate that it may be functionally potent. Cerebral blood vessel nerves may be the vestigial remains of a structural differentiation in ontogeny. The vermiform appendix contains many of the structural characteristics of the bowel, but functionally it is impotent. It is probable that some of the larger vessels at the base of the brain are somewhat more under vasomotor control than are the smaller vessels. Particularly, the myelinated fibers may be afferent, mediating sensation and certain reflex arcs.

Summary

Experimental factors are important in the evaluation of factors influencing vascular caliber of the pia. Heat from the light source may cause distention of pial vessels. Between systole and diastole pial vessels may change in size very slightly. With the use of a method which enables us to obtain photographs every thirty-second of a second, such changes are discernible.

1. The stimulation of the 5th, 6th, 7th, 9th, 10th, and 11th cranial nerves caused no change in the vascular caliber.

2. Stimulation of the vagus caused a bradycardia with initial slight increase in the blood pressure, followed by a fall, and increase in the pulse pressure during the stimulation. Immediately following the stimulation there was a 20% drop in the blood pressure. Stimulation of the central stump of the vagus and the peripheral stump of the seventh cranial nerve caused no change in the pial-vessel caliber.

3. Stimulation of the cervical and upper thoracic sympathetic chain and ganglia caused no change in the pial-vessel caliber.

4. Spasm of the pial vessels (40μ-150μ) was not seen in these studies. With adequate electrical currents, desiccation of the vessel with complete obliteration of its lumen was obtained. In other instances with a proper current a burn could be induced on the wall of the vessel without any change in its size. A neurogenic spasm of the vessel could not be demonstrated in our experiments.

5. Pial vessels can become distended or may contract due to mechanical effects of the cardiac output and to the inhalation of carbon dioxide or oxygen. Carbon dioxide

causes an unmistakable distention of the pial vessels of from 25% to 40%. Oxygen inhalation causes a contraction of the pial vessels of a less degree than that with the distention caused by carbon dioxide inhalation. About 10%-15% contraction of the vessel occurs with oxygen inhalation.

Species differences and anesthesia may be important factors in the differences between results described in this paper and the observations of others.

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Lumbar Extradural Cysts—Congenital

Their Proper Classification

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Congenital extradural spinal cysts are exceedingly rare and represent the least common cause of spinal cord pressure. The literature records only 35 cases. This fact, coupled with the satisfying surgical results, dictates the periodic review and discussion of the symptoms and diagnostic features. These extradural cysts have a high predilection for the thoracic region, 29 of the 35 reported cysts occurring entirely within the thoracic region. Six have been reported extending into the lumbar region, and of these only two have occurred *isolatedly* in the lumbar area.

The literature is consistent in reporting the symptomatology and signs of spinal extradural cysts as being compatible with an expanding lesion in the thoracic area. This description was initiated by Elsberg, in 1934, and has been quoted verbatim in several of the subsequent reports as follows:

> The individual is an *adolescent* with the history and symptoms of a progressive spastic paraplegia. *Pain is absent* or is not a prominent symptom. The objective disturbances of sensibility are slight and their upper level is in the mid-thoracic region, usually at the sixth or seventh thoracic dermatome. The manometric tests demonstrate a subarachnoid block with the characteristic spinal fluid changes of *cord* compression. Measurements on antero-posterior x-ray films show that the interpedicular spaces of three or more vertebrae, somewhere between the fourth and tenth thoracic vertebrae, are enlarged. The pedicles of the affected vertebrae especially those of the sixth, seventh and eighth, are narrowed and atrophic.

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This picture is the clinical syndrome of congenital spinal extradural cysts but in no way portrays the clinical picture in an extradural cyst of the lumbar area. Because of this difference, congenital cysts located extradurally in the lumbar area should be separated and better identified by the term congenital lumbar extradural cyst.

On the basis of a review of the six cases of cyst that have extended into the lumbar area and a correlation of these cases with a recent case in which the cyst originated in and was confined to the lumbar region, the symptomatology and clinical signs should include the following features:

The patient is not a male adolescent; instead, he may be an adult of either sex, in the 30's or 40's. The duration of symptoms is usually much more protracted, being measured in years, whereas the average duration of symptoms for cysts of the thoracic area is measured in months. The advanced age at onset and the long duration of symptoms obviously are explained by the cyst being located in and compressing predominantly the cauda equina rather than the cord and tracts. The patient complains of back pain; this is an infrequent complaint with the spinal cysts. The spine is straight. There is loss of the normal lordotic curve, and there is muscle guarding. This is in contrast to the dorsal kyphosis occurring with cysts in the thoracic region. The patient will have hip and leg pain, and there will be weakness, of gradual onset, with decreased reflexes in the roots involved. Paresthesias are uniformly noted in one lower extremity, as contrasted with the absence of paresthesias in the thoracic form. The patient has weakness of lower

motor neuron type, predominantly in one leg, with absent to diminished reflexes (Table).

Careful attention needs to be directed to the routine films of the spine. The characteristic findings are widening of the interpedicular space, thinning of the pedicle and lamina *opposite* the cyst, and slight cavitation of the posterior border of the body of the vertebra. As such findings are compatible only with an expanding lesion, myelography is frequently needed to portray the smooth outline of the extradural cyst.

The pathogenesis of the congenital cyst is that of a defect in the dura mater located lateral to the midline, more posterior than anterior. The dural defect is usually not more than 1 to 2 mm., through which protrudes and balloons the spinal arachnoid membrane, making for a spinal-fluid-containing, thin-walled cyst. This cyst fails to adhere to or form strong adhesions with the dura mater. The cysts are variable in size but usually extend more than two or three vertebrae. Because of this pathogenesis, this cyst often is referred to as spinal arachnoid diverticulum.

Report of a Case

Our interest in this subject was pointed up by the case of a 41-year-old white woman who had presented intermittent low-back pain for four years. On March 20, 1956, she was awakened about 1 a. m. with severe low-back pain with radiation into the posterolateral aspect of the left thigh. There were definite paresthesias. She stated: "It was something very hot inside of the back part of my left leg." Two weeks later she discovered numbness in the posterolateral aspect of the thigh and leg and over the top of the foot. Only after five weeks of bed rest and use of analgesics did she return to doing light housework. Four months later she had a similar severe attack, which failed to respond to conservative measures. She was admitted to the hospital on Aug. 15.

Her gait was awkward, and walking produced pain in the midlumbar area. There were muscle guarding and limitation of lumbosacral motion. There was a limp with weakness in the left lower extremity, and she could not stand on her toes or heels. There was tenderness of the spine at L2 and L3. The sciatic-elongation signs were positive on the left. Definite reduced sensation was elicited over the L3, L4, L5, and S1 dermatomes of the left extremity. There was atrophy of this extremity of 1 cm., as measured above and below the left knee. The left knee jerk was diminished, and the left ankle jerk was absent.

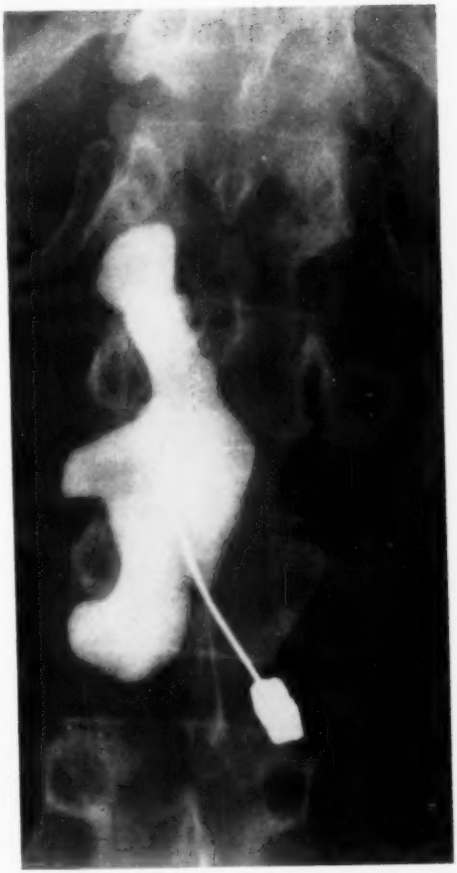

Fig. 1.—"Cystogram," anteroposterior view. Note the close approximation of the cyst to the lamina and the projection of the cyst through the intervertebral foramen. Note the thinning of laminae T12, L1, L2, and L3 on the right side.

X-ray studies showed osteoarthritic changes of the thoracic vertebrae commensurate with her age. The interpedicular spaces (Fig. 1) were 30 mm. at L1, 28 mm. at L2, and 26 mm. at L3. There was erosion of the right pedicle of L1. Lateral views showed the slight characteristic cavitation of the body of vertebra L2 and enlargement of the intervertebral foramen at L2.

Because of the extensive root signs, the 18-gauge needle was placed between the spines of L1 and L2. The measured pressure was 40 mm. of water.

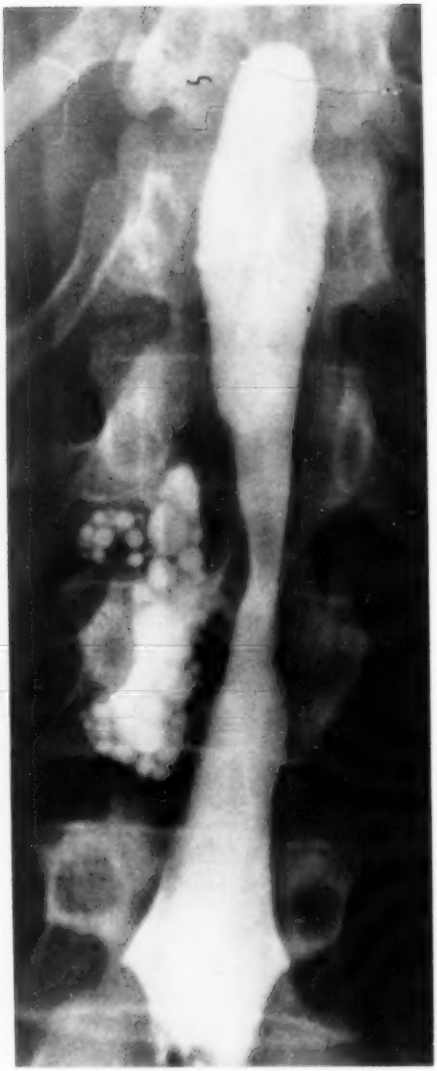

Fig. 2.—Myelogram, anteroposterior view. Note the residual oil in the cyst from the preceding day. There is a fusiform extrinsic filling defect extending from the inferior border of T12 to the middle of the body of L3.

Bilateral jugular compression caused a slow rise in pressure to 75 mm. We removed 8 cc. of clear fluid, and 6 cc. of iophendylate (Pantopaque) was injected. The fluid contained 4 cells per cubic millimeter and 20 mg. % of protein, and the Pandy reaction was clear. Fluoroscopically, the oil was seen to be loculated predominantly on the left, extending from the L1 to the L3 interspace. It seemed to protrude between and around the pedicles of L1 and L2. The entrapped opaque oil would not gravitate on tilting the patient. Because of this abnormal situation, 5 cc. of the oil was removed and fluoroscopy was repeated. The residual 1 cc. of iophendylate remained loculated, and we again instilled 5 cc. of iophendylate. Identical fluoroscopic studies and films were obtained, and it was clear that a "cystogram" had been obtained (Fig. 1). As much as possible of the iophendylate was withdrawn. The patient was encouraged to ambulate and to be up for the next 48 hours. Her symptoms were clearing.

A myelogram seemed indicated, and 48 hours later a new study was performed. Preliminary scout films were taken—the residual oil remained. The needle at this time was placed in the L4-L5 interspace. The CSF pressure was measured at 160 mm.; with bilateral jugular compression, the pressure rose steadily to 280 mm. The CSF was of normal appearance. Six cubic centimeters of iophendylate was injected, and the oil column was seen to be thinned out and to be displaced to the right at L1, L2, and L3 (Fig. 2). The concave border of this defect was smooth and corresponded to the outline as seen on the "cystogram."

After discussion with the patient, a laminectomy was decided upon. The spines and laminae of L1 and L2 were removed out to the articulating facets bilaterally. The lamina was decidedly thinned on the right at L1 and L2. There was no extradural fat. Immediately below the lamina, in the left posterior quadrant of the canal, was found a thin-walled sac, which extended from the lower border of T12, caudally, to the lower border of the lamina of L3. This compressible sac protruded through the interlaminal space between and around the pedicles of L1 and L2. After delineation, the sac was seen to pouch into the neural foramina (Fig. 3). The sac, which had the gross appearance of thin-walled dura, was punctured, and 5 cc. of clear fluid mixed with iophendylate was obtained. This partially collapsed the sac, which was then readily lifted from the dura. The sac was opened and completely evacuated (Fig. 3). The pedicle of the sac came off just superior to the emergence of the left second lumbar root. A silk suture was placed around the pedicle, and the sac was resected. Because of the myelographic finding of nerve root compression at the S1 root, it was felt advisable to do an interlaminal exploration and inspect the S1 root. This was accomplished through a lower incision with the same anesthesia. There seemed to be a moderate lateral protrusion of the disk of L5, sufficient to account for the myelographic defect. The left S1 nerve root was adequately decompressed and both wounds closed. The patient did well postoperatively, being discharged on the seventh postoperative day. Her preoperative com-

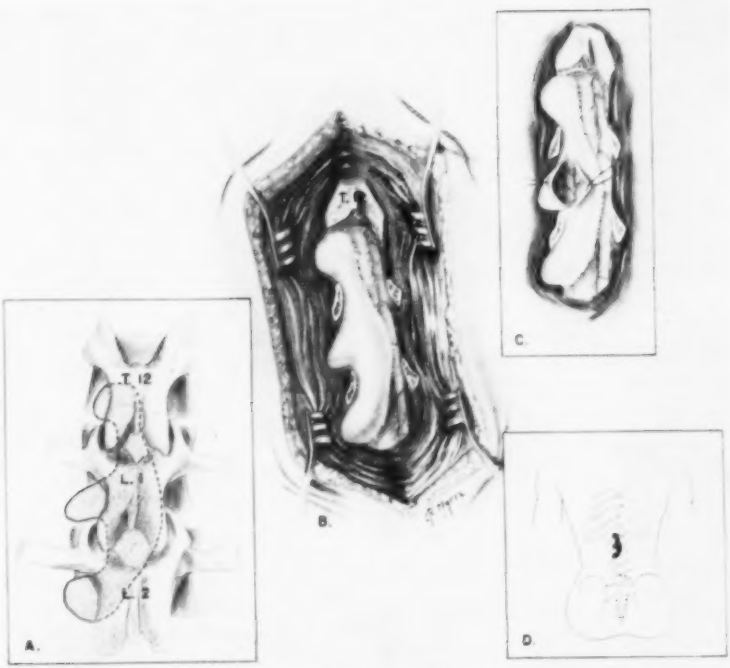

Fig. 3.—(*a*) Operative sketch of cyst in relationship to vertebra. (*b*) Appearance of cyst after removal of spines of T12, L1, and L2, and lamina of L1 and L2. (*c*) Cyst opened and evacuated. (*d*) Topographical location of cyst.

plaints and symptoms disappeared after surgery, and she has remained symptom-free to date. She has increased strength in the left lower extremity, and the paresthesias are no longer present over the thigh and leg.

Comment

The similarity of the syndrome with that of a protruded lumbar disk should be emphasized. Four of the patients with cysts extending into the lumbar area were first considered to have a ruptured disk. In the case reported by Wise and Foster,[8] the patient had surgery for a lumbar disk, but the symptoms remained and increased; the authors reoperated with a laminectomy and found the cyst seven weeks later. The long duration and intermittent character of the symptoms and the root distribution of the lower motor neuron signs can be misleading.

The presence of a complete or near-complete spinal subarachnoid block secondary to a mass lesion is usually aggravated by the removal of spinal fluid. This is not true in case of the spinal extradural cyst, in which there is striking improvement in the subjective complaints and in the neurological deficit. Such a finding assists in the differential diagnosis. The explanation for this is that the cyst mass is allowed to be decompressed or to assume a more elongated shape, with less embarrassment of the canal space.

The present case is the first reported instance in which the manometrics within the extradural cyst were obtained in an *intact* spinal canal and these values compared with the subarachnoid manometrics.

The unique incident of a contrast substance having been placed preoperatively in the cyst and allowed to remain in the cyst with motion, etc., in the usual manner on the part of the patient may give some idea of the pathological mechanics of ex-

Findings Which Show the Extreme Contrast Between Spinal and Lumbar Extradural Cysts

Findings	Lumbar Extradural Cyst	Spinal Extradural Cyst
Age	40 yr.	14 yr.
Sex	Divided	Male
Duration	Years	Months
Motor	Weakness—mild lower motor neuron type	Upper motor neurone type, more rapid and severe
Reflexes	Hypoactive to absent	Hyperactive
Back pain	Prominent	Slight, if any
Paresthesia	Present, usually in one leg	Not usual
Hip and leg pain	Usual	Not usual
Sensory loss	Root distribution	Tract distribution
Kyphosis	Not present	Present
Spinal block	Not present	Present

tradural cysts; that is, there must be a very restricted communication between the cyst and the subarachnoid fluid which prevents a free exchange, as demonstrated by the failure of the iophendylate to escape from the cyst.

The erosion of the laminae and pedicle in the lumbar cyst is on the side opposite that of the cyst (Figs. 1 and 2). This is due to the cyst (Fig. 2) being protected by the cushion of the lower-pressured cyst. We believe this to be in contrast to the condition in other mass spinal lesions and to that in the spinal (thoracic) extradural cysts.

A tabulation of the common findings in those cysts which have extended into the lumbar area (Table) shows the consistency of the symptomatology and signs, of sufficient degree that such lesions should be grouped together and identified as lumbar extradural cysts. The Table shows the extreme dissimilarity of the findings based on the anatomical location of the cyst above the level of L1. Lesions showing such an antithesis of findings should not be collectively called spinal extradural cysts. The term spinal extradural cyst, which is firmly established in the literature, should be retained for those lesions of the cervical and thoracic regions. To avoid confusion, those cysts anatomically located below L1 should no longer be included in a diagnostic class that fails to convey their symptomatology. They should be termed lumbar extradural cysts.

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Effect of Blood Plasma from Psychotic Patients upon Performance of Trained Rats

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A variety of biochemical abnormalities has been described in schizophrenia. These include changes in glucose metabolism,[1] in adrenocortical physiology,[2] and in blood histamine,[3] ketones,[4] and glutathione.[5] Abnormal urine metabolites have also been described.[6-8] Weichbrodt[9] reported that the blood plasma from psychotic patients was toxic for mice, and Fischer[10] found it to be toxic to the larvae of Xenopus laevis. The latter conclusion has been disputed.[11] Shapiro[12] reviewed the literature on attempts to find a toxic substance in cerebrospinal fluid of schizophrenic patients; he was unable to detect such a factor when cerebrospinal fluid was injected subcutaneously into rats. Leach and co-workers[13] found that the plasma in schizophrenia and certain other diseases oxidize epinephrine more rapidly than normal, and they have obtained a factor from the plasma of schizophrenics which is said to be qualitatively different from normal ceruloplasmin.[14] They have given the name "taraxein" to this factor.

For several years, we have maintained a colony of trained rats whose performance has been found to be quite sensitive to drugs affecting the central nervous system,[15] especially to lysergic acid diethylamide (LSD).[16] It occurred to us that if there were a toxic factor affecting the central nervous system in the plasma of schizophrenic patients, it might be possible to demonstrate it in this preparation. The present report deals with the effect of whole blood plasma injected intraperitoneally into these trained rats.

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Merck Institute for Therapeutic Research.

Methods and Materials

Holtzman male rats of about 100 to 200 gm. body weight were trained to climb a vertical rope a distance of 172 cm., as previously described.[15,16] The animals were fasted 24 hours or more; a food cup on a platform at the top of the rope was an incentive to climbing. Climbing time (C. T.) was determined to the nearest 0.1 second. Three control determinations of C. T. were made before injection. The animals then received intraperitoneal injections of 1 ml. of serum or plasma. Heparinized plasma was used in most of the experiments, but a few were performed with serum; this seemed to make no difference, and so no distinction is made between serum and plasma in this report. Control animals received injections of saline or heparin solution.

After injection, C. T. was tested at intervals of 15 minutes for the first hour, and 30 minutes thereafter until performance had returned to the base line. The experiment was usually terminated after three hours, even in those animals which had not yet returned to normal performance. In addition to measurements of C. T., observations were also made of the behavior of the animals, both in their cages and on the rope. When C. T. was plotted against time after injection, a polygon was formed whose area could be readily calculated. The effect of a given treatment could be determined by its effect upon the area of the polygon. The unit of area of the polygon has been termed the "minute-second,"[17] since the ordinates are in seconds and the abscissae are in minutes. For purposes of calculating this area, an animal failing to negotiate the climb within 60 seconds is arbitrarily assigned a C. T. of 60 seconds. The "climbing time delay" (C. T. D.), in minute-seconds, is essentially the product of the intensity of the effect of treatment and the duration of such effect. This concept has been explained in previous publications.[16,17]

Plasma from psychotic patients was obtained from patients, most of whom were not on ataractic drug therapy, from three different sources: Veterans' Administration Hospital, Coatesville, Pa.; Psychiatric Division of Bellevue Hospital Center, New York, and Norristown State Hospital, Norristown, Pa. Experiments on the plasma of patients from the first two were performed in the labora-

tories of the Merck Institute for Therapeutic Research, Rahway, N. J., and the Norristown samples were tested at West Point, Pa. Control plasma was obtained from staff members and nonpsychotic patients at the above-mentioned hospitals and from patients in the Medical Division at Bellevue Hospital, Rahway Memorial Hospital, and Pennsylvania Hospital, Philadelphia.

Animals were never used more than three times, usually with at least a week's rest between experiments. In the majority of cases in which the animals were re-used, those previously receiving psychotic plasma were given normal plasma and vice versa. Usually there was enough plasma to treat three rats, but in a few cases only one or two rats were used on a given sample.

There was considerable variability in the response of different rats to the same plasma. The degree of variation was proportional to the average C. T. D. Therefore, in order to normalize the data and to make the variances more homogeneous, a statistical device known as the square-root transformation was employed: After the response of each rat had been calculated (C. T. D. in minute-seconds), the square root of the C. T. D. was extracted. The mean value of the square roots for all the animals treated with each individual plasma specimen was then obtained; the square of this figure was taken as the response to that particular plasma specimen. This manipulation of the data did not markedly affect the values obtained, but facilitated statistical handling of the data.

Results

Effect of Intraperitoneal Injection of Plasma.—Altogether, plasma specimens were used from 80 different patients nominally psychotic (mostly schizophrenics) and from 82 nonpsychotic subjects. The latter can be divided into two groups, 35 general hospital patients, with a variety of diseases, and 47 presumably normal volunteers. For convenience, these groups will be referred to in this paper as "psychotic," "physically ill," and "normal." It is recognized that there may be some overlap among these groups. The first group consists of patients in mental hospitals, but their disorders may be of diverse etiologies, and their confinement within institutional walls may be their only common denominator. The last two groups were not examined psychiatrically,

TABLE 1.—*Effect of Intraperitoneal Injection of One Milliter of Blood Plasma from Psychotic and Other Subjects upon the Performance of Trained Rats*

	Psychotic Patients			Other Patients			Normal Subjects		
Experiment No.	Source*	No. of Samples	Av. C. T. D. Min.-Sec.	Source*	No. of Samples	Av. C. T. D. Min.-Sec.	Source*	No. of Samples	Av. C. T. D. Min.-Sec.
1	C	6	1253	—	0	—	C	4	170
2	C	5	949	—	0	—	C	2	262
3	C	1	172	C	2	156	C	3	22
4†	C	2	6	C	1	8	C	2	1
5†	B	6	2025	R	6	262	R	2	49
6	B	2	85	B	4	27	B	3	135
7†	B	4	3260	B	6	64	—	0	—
8	B	3	480	R	3	49	—	0	—
9	—	0	—	R	8	132	—	0	—
10	N	3	256	—	0	—	N	3	193
11	N	3	243	—	0	—	N	3	128
12	N	3	69	—	0	—	N	3	48
13	N	4	303	—	0	—	N	2	125
14	—	0	—	—	0	—	N	5	59
15	N	3	328	—	0	—	N	3	48
16	N	3	369	—	0	—	N	3	185
17	N	3	190	—	0	—	N	3	328
18	N	3	313	—	0	—	N	3	266
19†	N	5	350	—	0	—	N	1	42
20	N	4	169	—	0	—	N	2	185
21	N	8	474	—	0	—	—	0	—
22†	N	9	262	P	5	61	—	0	—
Total		80	677		35	100		47	133

* Sources: C = Veterans' Administration Hospital, Coatesville, Pa.; B, Bellevue Hospital; R, Rahway Memorial Hospital; N, Norristown State Hospital; P, Pennsylvania Hospital.

† In Experiments 4, 5, 7, 19, and 22, specimens were run on two or more different days. Otherwise, in each experiment all specimens were tested on the same day.

and may well include persons with histories of mental illness, or even with mental disturbance concurrent with taking the blood sample. Indeed, in a few instances there is reason for believing this to be the case. However, in the absence of any more definite criteria, it was decided to retain the classification in the three groups and accept the overlap of data which this might entail.

As Table 1 shows, the data can be conveniently divided into 22 experiments. Both psychotic and one or more of the other types of plasma were included in 19 of these. The psychotic plasma had a greater effect than the others in 15 of the 19 experiments. The highest average effect obtained in any of the tests for nonpsychotic plasma (normal plasma, Experiment 17) was exceeded in eight of the experiments by the psychotic samples. There were 16 experiments in which psychotic and other samples were directly compared on the same day (this includes part of Experiments 7 and 19). In 13 of these experiments, the highest value was obtained from the psychotic plasma. There is about 1 chance in 100 that this can happen by chance when there is no real difference, $P=0.01$.[21]

It will be noted that the over-all average of the effects of the psychotic plasma was 677 min.-sec., as compared with 100 and 133 min.-sec. for the physically ill and the normal groups, respectively. These averages are probably unduly high because of a few samples that gave unusually high results. The corresponding medians are 374, 88, and 96 min.-sec., respectively. Of the 80 psychotic samples, 68, or 85%, had values above the median for the normals, while 94% of the specimens from physically ill patients and 91% of the normals were below the median for the psychotics. Also, 85% of the psychotic samples gave a higher value than the normal mean, while 98% of the normal samples and 94% of the specimens from the physically ill gave a lower value than the psychotic mean. This indicates that the plasma of psychotic patients had a very different effect upon the performance of the rats than did that from the other two groups, which did not differ significantly from each other. Eight of the patients were known to have received chlorpromazine, but none for at least 24 hours before blood was drawn. There was nothing in the results obtained with these samples to set them apart from the other plasma specimens from psychotic patients.

The illnesses of the 35 ill patients not classified as psychotic were as follows: brain trauma, 1; emotional instability, 2; advanced senility, 4; nephritis, 1; obstructive jaundice, 2; diabetes, 3; cardiovascular conditions, 5; both diabetes and cardiac ailment, 2; rheumatic fever, 1; tonsillectomy, 1; high basal metabolic rate (probably due to hyperthyroidism), 1; condition undiagnosed, with very high blood nonprotein nitrogen, 2; subacute bacterial endocarditis, 1; diverticulitis, with bowel resection (postoperative), 1; biliary cirrhosis, 1; myasthenia gravis, 1; diagnosis not available at this writing, 6. Of these 35, the samples of 2 had an effect greater than the median effect of the psychotic plasma. One of these was a case of very advanced senility, and the other was said by the technician who drew the blood to be irrational, and seemingly not normal mentally.

The data have been analyzed by a number of statistical approaches. For all the Coatesville material (Experiments 1-4), the mean values were as follows: psychotics 1167 ± 358 min.-sec., nonpsychotics (both groups) 139 ± 44 min.-sec. The difference is significant, $P<0.01$. Similarly, for the psychotic samples obtained from Bellevue (Experiments 5-8), the mean was 1912 ± 411 min.-sec. as compared with 133 ± 46 min.-sec. for the corresponding normals; $P<0.001$. For the Norristown material (Experiments 10-13, 15-20), the means were 354 ± 58.1 and 142 ± 24.1 min.-sec.; $P=0.0014$. Thus, in each set, the difference between psychotic and normal plasma was highly significant.

Figure 1 shows the distribution of all the data. It will be noted that the plasmas of

Distribution of data on the effect of intraperitoneal injection of 1 ml. of blood plasma on the performance of trained rats. Solid line, distribution of data from the 47 normal samples; broken line, data from 80 psychotic samples; dotted line, data from 35 nonpsychotic patients. The difference between the psychotic group and the other two groups is highly significant, $P<0.001$.

most of the "normal" and "physically ill" cases (51% and 54%, respectively) fall within the lowest group, i. e., little or no effect on the performance of the rats. Most of the data from psychotic patients (59%) occur in the upper two classifications, i. e., a marked effect on performance. The χ^2 test on the difference in distribution between normals and psychotic subjects shown in Figure 1 gave a value for χ^2 of 30.4 (*d. f.* = 4); $P<0.001$.

The material from Norristown State Hospital (Experiments 10-21) was better adapted to statistical evaluation than the others. These samples were all drawn by the same technician at the same time of day and were submitted to the experimenter by number only.* On most days, plasma from both normal and psychotic patients were included, but the experimenter did not know which was which until after the experiment had been run. In Experiments 10-17, the test was performed on the same day that the blood was drawn; the other samples were frozen for varying lengths of time. A preliminary analysis of these data showed that the deviations from experiment to experiment were not greater than those within experiments; therefore, all the Norristown data could be considered as one experiment for statistical purposes. An analysis of variance was therefore performed, and is shown in Table 2. This demonstrates a highly significant difference between psychotic and normal subjects ($P<0.001$).

The difference in ranges of individual values in the two sets of Norristown data (34 to 1592 min.-sec. for psychotic plasma; 6 to 520 min.-sec. for normal plasma) was sufficiently large to suggest that nonparametric methods of evaluation might be indicated. Using the rank test of Kruskal and Wallis,[18] the average rank value for the psychotic samples was 50.1 min.-sec. and for the normals 30.3 min.-sec. The difference is highly significant, $P=0.0002$. The Rosenbaum Test of Location[19] was also applied to the Norristown data. Of the 34 normal plasma values, 6 were lower than the lowest for psychotic plasma, $P<0.01$, and 8 of the 49 psychotic plasma values were higher than the highest for normal plasma, $0.05>P>0.01$.

In an additional rank evaluation of the 16 paired experiments in which psychotic and normal plasma samples were run on the same day, it was estimated that the probability of the observed rank total occurring by chance was $P=0.001$.[21]

Therefore, it is quite clear that intraperitoneally administered blood plasma from at least a large proportion of psychotic patients exhibits a toxicity in trained rats which cannot be demonstrated in the plasma from a majority of normal subjects.

Behavior of the Rats.—In addition to determinations of climbing times, notes

TABLE 2.—*Analysis of Variance on Data from Experiments 10 to 21, Inclusive*

Source of Variation	*d. f.*	Sums of Squares	Mean Square	*F*
Psychotics *vs.* controls	1	534.19	534.19	11.97*
Error	72	3212.78	44.62	
Total	73	3746.97		

* Very highly significant, $P<0.001$

* Dr. W. P. Boger made these arrangements possible.

were also taken of the behavior of the animals. Our rats are accustomed to being handled and are very docile. When the cage door is opened, they normally crowd forward to the door and eagerly sniff at the observer. When placed on the electric grid at the bottom of the rope, they instantly jump onto the rope and proceed upward by a series of leaps, advancing both forepaws at once, then both hindpaws. When they reach the platform at the top of the rope, they immediately go to the food cup and start eating. The animals which have received normal plasma usually show nothing abnormal in their behavior, except sometimes some sluggishness while climbing. The more potent of the plasma specimens from psychotic patients, however, produced marked changes in behavior. The animals tended to remain quiet and huddled in their cages, as though they had received a hypnotic drug. When the cage door was opened, instead of coming forward to meet the observer, they retreated to the back of the cage, withdrawing as far as possible from the experimenter. When placed on the grid, they would sometimes take several shocks before jumping onto the rope. Once on the rope, they would often stay in one place and remain motionless as though staring into space. When attempting to climb, there were often fumbling movements of the forepaws. Progress upward was achieved by advancing one paw at a time, instead of the normal leaping motion. If successful in climbing the rope, they would often hang their heads over the food cup without eating. Much of this behavior is reminiscent of that previously described as a result of LSD intoxication,[16] though it lacks some of the features of the latter.

An occasional plasma sample produced powerful abdominal contractions when administered intraperitoneally. This was seen with several normal, as well as psychotic, specimens and did not always affect the behavior or performance of the rats. The plasma component causing this is unknown. A similar phenomenon has been observed after injection of various drugs, including serotonin.[16]

Effect of Route of Injection.—Shapiro[12] did not detect any effect of cerebrospinal fluid from catatonic patients when injected subcutaneously in rats. Since our results had been obtained with intraperitoneal injection, we obtained 15 specimens of psychotic plasma in sufficient quantity to test both by subcutaneous and by intraperitoneal routes two to three rats receiving 1 ml. of each specimen by each route. All the specimens gave negative results by the subcutaneous route, but when injected intraperitoneally 13 of the 15 produced an effect above the over-all median for the animals receiving normal plasma. As a group, these were quite active samples when given intraperitoneally (mean effect, 983 min.-sec.), but the response after subcutaneous injection (21 ± 34.3 min.-sec.) did not differ significantly from that of intraperitoneal 0.9% sodium chloride (2 ± 2.0 min.-sec., mean of 61 trials). It appears likely that the toxic factor may not be absorbed sufficiently rapidly after subcutaneous administration to exert the effect seen by the intraperitoneal route. We have no data on intravenous or oral administration.

Comparison of Plasma and Cerebrospinal Fluid.—Several attempts have been made to demonstrate a toxic factor in cerebrospinal fluid of psychotic patients, with inconsistent results.[12] We have obtained from Norristown State Hospital simultaneous plasma and cerebrospinal fluid specimens on six patients and tested them by injection of 1 ml. intraperitoneally in our rats. The results are shown in Table 3. Four of the six plasma samples markedly affected the performance of the rats, while only one of the cerebrospinal fluid specimens had a moderately positive effect (Patient 4), and this was considerably less than that of the plasma of the same patient. The toxic factor, therefore, if present in cerebrospinal

TABLE 3.—*Comparison of Effect of Plasma and Cerebrospinal Fluid on Performance of Trained Rats*

Patient No.	Plasma		Cerebrospinal Fluid	
	No. of Rats	Av. C. T. D., Min.-Sec.	No. of Rats	Av. C. T. D., Min.-Sec.
1	3	912	3	83
2	3	149	3	56
3	3	40	1	0
4	3	428	3	246
5	3	392	3	64
6	3	331	3	114

fluid, must be in too low a concentration to be detected by the methods used.

Repeated Observations on the Same Patients.—If we are correct in our view that our method detects an abnormality in the plasma of the majority of psychotic patients, the abnormality should be detectable in a repeat sample taken at a later date, if the patient remains ill. Therefore, we have obtained second samples on 10 psychotic patients, 3 of whom gave negative results on the first trial. The results are shown in Table 4. It is evident that all of the second samples gave results well above the median value for normals, and only one sample (Patient 72) produced a rather low response. There was no correlation between the absolute values obtained in the two trials, but this was not to be expected, in view of the variability among rats. It is worthy of note that the three patients who gave negative results on the first trial gave positive results the second time. This raises the interesting possibility that repeated determinations might achieve an almost complete separation between psychotic and normal subjects. As mentioned above, there was considerable variation in the response of different rats to the same sample. It is not unlikely, then, that when only two to three rats are used for each sample, the group might consist of all unresponsive rats and hence give a negative result, even for an active specimen. The extraordinarily high value obtained for Patient C in the first trial was not repeated on the second trial, but the result was still above that usually obtained from plasma of nonpsychotic subjects.

The data from the first trial of these 10 patients have been included in the over-all statistical evaluation of the results given in a preceding section of this paper, but the data from the second trial were not included.

Relation Between the Diagnoses and the Results of the Rat Test.—In Table 5 are listed the diagnoses which were supplied to us, along with the samples submitted for the 80 patients from the three psychiatric hospitals. The diagnoses are listed as given by the hospitals supplying the samples, with no effort to correlate any possible differences in classification by the different hospitals. In all classes, median values well above those of the control groups were obtained. The apparent quantitative differences among the classes are probably not

TABLE 4.—*Repetition of Observations on Plasma Drawn from Psychotic Patients on Different Dates*

Patient	First Sample		Time Interval	Second Sample	
	No. of Rats	Av. C. T. D., Min.-Sec.		No. of Rats	Av. C. T. D., Min.-Sec.
1	3	34	6 mo.	3	240
55	3	34	5 mo.	3	529
74	2	77	3 mo.	3	234
30	3	424	6 mo.	3	458
A	3	428	6 da.	3	471
72	3	502	5 mo.	3	159
53	3	511	5 mo.	3	520
57	3	718	5 mo.	3	286
B	3	912	12 da.	3	243
C	3	4058	16 da.	3	260

TABLE 5.—*Diagnoses of Eighty Patients from Three Psychiatric Hospitals Used in This Study*

Group	Diagnosis	No. of Patients	Median C. T. D., Min.-Sec.
I	Schizophrenia, paranoid	16	491
II	Schizophrenia, catatonic	12	311
III	Schizophrenia, childhood	3	172
IV	Schizophrenia, hebephrenic	4	260
V	Schizophrenia, undifferentiated or not specified	26	337
VI	Manic-depressive psychosis	4	295
VII	Alcholic psychosis	3	949
VIII	Mental deficiency with psychosis	4	295
IX	Chronic brain syndrome with psychosis	3	502
X	Miscellaneous	5	858

significant, as some of the groups are small in number and the ranges overlap. Of the schizophrenics, five were listed as actively hallucinating when samples were drawn. There was no difference between these and other schizophrenics.

The five patients included in the miscellaneous group (X) were severely ill, though it is not certain that they should be considered psychotic. The diagnoses supplied with these samples were as follows: "paranoid," 1; "passive-aggressive," 2; "kleptomania with possible schizophrenia," 1, and "grand mal epilepsy with neurosis," 1. The reactions which we observed in the rats would indicate they fit in with those subjects classed as psychotic.

Comment

The data established beyond any doubt that blood plasma from psychotic patients affects the performance of our trained rats and that this action is at least quantitatively, and possibly qualitatively, different from that elicited by plasma of nonpsychotic subjects. There are some overlap and variability of results, but the over-all trend is clear. The behavior of the animals and the points of similarity of the observed syndrome to that described for LSD[16] suggest that the toxic action is on the central nervous system, though the experiments do not unequivocally establish the site of action. If it is in the central nervous system, then it might be appropriate to refer to the active substance or substances as "psychotoxic."

The work of the Tulane group[13,14] suggests that the abnormal factor in psychotic plasma may be enzymatic. If so, then the effect on any one of our rats might depend upon the presence of the appropriate substrate in the animal. We have no clue as to what this might be, but if it were variable from animal to animal or if an inhibitor were present in some animals, the variation in susceptibility of the rats to the same plasma specimen would be explainable. Furthermore, we are working with relatively small amounts of plasma and have not concentrated it; so for most plasma samples we are using nearly threshold quantities, further accounting for the variability. With several of the samples, smaller amounts (0.5 cc.) were tried, and only the most highly active ones had any effect.

Since we do not know the nature of the hypothetical "psychotoxic factor," we also do not know the optimal conditions for collecting or handling the plasma, and this is a possible source of variability among specimens, aside from their actual differences. Schizophrenia is probably not a single disease, but has several subdivisions. The patients may manifest their difficulties in diverse ways, and the etiologic factors may be equally diverse. There appears to be a toxic factor in the plasma of schizophrenics and of other psychotics, but there is no assurance that it is identical in all cases. There may be a variety of such factors.

In view of the many sources of possible variations, it is perhaps remarkable that the difference observed between psychotics and nonpsychotics is as clear-cut as it is. We have not been able to control all the variables mentioned by Horwitt,[20] but our results seem not to be due to an artifact. With regard to emotional stress in nonpsychotic patients, we have included among our controls a number of seriously ill general hospital patients, some of whom were

undergoing the severe emotional stress of a preoperative state, but none of these specimens affected our rats as did the psychotic samples.

The factor of long-continued inactivity on the part of patients confined for many years in mental institutions also can be ruled out as a source of error in our findings. Both chronic and acute cases are included in our data, and some of the psychotic samples were obtained upon first admission to the hospital, even before a firm diagnosis had been made. These specimens affected our rats at least as much as did those of the patients who had been ill for years, and who were in a state of acute exacerbation of symptoms. Our information does not include the degree of chronicity for all the patients, but the patients for whom we do have such information include both acute and chronic cases; we did not detect a significant difference between the two. The chronic cases should probably be further subdivided into the so-called "deteriorated schizophrenics" and those who have made some adjustment to institutional life and who may not currently be showing many signs of their illness. However, our information does not permit analysis of these categories.

We cannot be certain that the nutritional status of the psychotic and nonpsychotic subjects was identical. However, it is quite likely that populations of subjects as large as those we have used in this study may include a range of nutritional states in both the psychotic and the nonpsychotic group. A number of the nonpsychotic subjects were grossly abnormal metabolically: Five were diabetic; two had very high plasma nonprotein nitrogen; one had an elevated B. M. R. Six of these eight patients gave negative results in the rat test; one of the remaining two patients, a gravely ill diabetic, gave a borderline response, and the other was the patient mentioned above who gave a positive response and who was noted to be "irrational." Horwitt [20] also mentions the possibility of liver dysfunction being responsible for biological differences between psychotics and nonpsychotics. Three of our controls were jaundiced; all of these gave negative results in the rats. We conclude that whatever metabolic disorders led to the observed abnormality in the psychotic subjects, they must have been different from those seen in the somatically ill patients.

The substance or substances in the psychotic plasma responsible for the results we have obtained remain to be identified. It is hoped that further investigation will establish the fraction of the plasma containing the toxic material, the identity of the substance, its biological properties, and methods of antagonizing its action. Our findings do not establish an etiologic relationship between the toxic factor and the symptomatology of the psychoses. This relation, if any, remains for future research.

Summary

Intraperitoneal injection of blood plasma from the majority of schizophrenic and other severely psychotic patients into rats produced a syndrome resembling, but not identical with, that produced by injection of LSD. In rats trained to climb a rope, the injection of 1 ml. of plasma produced a deficiency in performance which could be objectively and quantitatively measured. Comparisons of the effects of plasma from 80 psychotic patients and 82 nonpsychotic subjects, including both general hospital patients and normal subjects, showed a marked and highly significant difference between the two groups. Cerebrospinal fluid had much less effect than plasma.

The following persons supplied us with the plasma samples: Dr. Herbert Sprince, Research Biochemistry Unit, Veterans' Administration Hospital, Coatesville, Pa.; Dr. Arthur Zitrin and Dr. G. L. Nicklin Jr., Bellevue Psychiatric Hospital, New York; Dr. Dickinson W. Richards, Bellevue General Hospital, New York; Dr. Alexander Kushner, Rahway Memorial Hospital, Rahway, N. J.; Dr. B. Gilmore, Pennsylvania Hospital, Philadelphia, and Dr. William P. Boger, Norris-

town State Hospital, Norristown, Pa. Mr. J. L. Ciminera gave assistance in statistical analysis of the data.

Merck Institute for Therapeutic Research.

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Society Transactions

LOS ANGELES SOCIETY OF NEUROLOGY AND PSYCHIATRY

James E. McGinnis, M.D., Presiding

Regular Meeting, Sept. 18, 1957

Reading Disabilities. Dr. Margaret E. Bransom.

Specific reading disabilities should be differentiated from alexia as a symptom of aphasia. The exact etiology of reading disabilities is not known. There are theories which range from the completely organic to the completely emotional. Early recognition is of great importance. Ability to read is less than is expected for the child's level of intelligence. There is a tendency to reverse letters, syllables, and words. From 84% to 94% of affected children are boys. Parents should be advised that ambidextrous children are more likely to need reading tutoring than children with early strong lateralization. Differentiation must be made between a specific reading disability with concomitant neurological disabilities and widespread neurological or personality disorders with an associated reading disability. Early and intensive tutoring is the greatest single aid in treatment.

Ataxia-Telangiectasia: A Familial Syndrome of Progressive Cerebellar Ataxia. Dr. Robert P. Sedgwick and Dr. Elena Boder (by invitation).

Over the past seven years we have independently observed seven children from five nonrelated families who presented a strikingly similar picture of progressive cerebellar ataxia associated with progressive oculocutaneous telangiectasia. In addition, a deceased sibling of one of the affected children almost certainly suffered from the same disorder. We have also had the privilege of seeing two other affected children in clinical presentations (Buchanan, Centerwall). Four more cases were presented at the First International Congress of Neurological Sciences in Brussels in July, 1957 (A. Biemond). Review of the literature has produced three more probable cases (Louis-Bar, Wells, and Shy). This makes a total of 16 cases known to us, all but 1 having been described in the past year.

The primary clinical characteristics of the syndrome are progressive cerebellar ataxia with onset in infancy; oculocutaneous telangiectasia, which is progressive and of characteristic distribution; frequent sinopulmonary infections; familial incidence; peculiarities of eye movements; normal intelligence, and retardation of statural growth.

One autopsy has shown apparent primary, chronic, and progressive cerebellar atrophy, involving principally Purkinje cells, granule cells, and basket cells.

The association of the telangiectasia and the cerebellar atrophy is not understood. Treatment is supportive only.

Subtentorial Vascular Anomalies: Malformations and Neoplasms. Dr. Cyril B. Courville.

The current literature contains many references to vascular malformations and anomalies of the brain since the appearance of the monograph on this subject by Cushing and Bailey. Relatively few of these contributions have to do with the lesions of this type which occur in the posterior fossa. This study was based upon the individual subtentorial vascular anomalies, malformations, and neoplasms found in the records of the Cajal Laboratory of Neuropathology. Upon the information gained from this material the following classification is based:

A. Vascular anomalies and malformations
  1. Isolated telangiectases of cerebellar white matter (at times associated with similar lesions in the cerebrum)
  2. Generalized meningocerebellar telangiectases (posterior fossa counterpart of Rendu-Osler-Weber disease)
  3. Capillary angioma of the pons
     (*a*) Isolated lesion
     (*b*) One of several angiomas of the brain
  4. Racemose angiomatous malformations
     (*a*) Pons (exterior aspects)
     (*b*) External surface of cerebellum
     (*c*) Cerebellar peduncles

B. Aneurysmal dilatations
  1. Saccular—congenital
  2. Fusiform or bulbous—arteriosclerotic

C. Vascular neoplasms
  1. Hemangioblastoma, cystic or solid, of the cerebellum (a counterpart of supratentorial angioblastic meningiomas)
  2. "Angioendothelioma" of the petrous bone and cerebellopontile angle (counterpart of angiomas of cranial vault)

It will be seen that in most instances subtentorial vascular anomalies and malformations are in all respects similar to lesions in the supratentorial space. One peculiar variant is what seems to be meningocerebellar telangiectases associated with progressive cerebellar symptoms occurring in children. This disorder resembles closely the supratentorial lesions found in Rendu-Osler-Weber disease (familial aspects, isolated small telangiectases in the skin). It differs in the absence of the tendency to bleed from associated lesions in the mucous membranes and viscera, but fossa have no identical counterparts in the supra- rarely from lesions in the brain.

In contrast, vascular neoplasms of the posterior tentorial space but are there represented by angiomatous or angioblastic meningiomas.

LOS ANGELES SOCIETY OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, Oct. 16, 1957

Autonomic Nervous System Tests as a Prognostic Guide in Various Physiologic Therapies in Psychiatry. DR. JOHN D. MORIARTY.

Since there is a vast body of data to confirm the assumption that psychologic and physiologic reactions are inseparable, investigations have been carried out to discover the correlations between relatively simple tests of autonomic nervous system responses and clinical psychiatric syndromes. The particular aim has been to aid in the selection of the modality of physiologic therapy ("somatic therapy") and to improve the clinician's predictability of the response to treatment.

Thus far the reaction of the basal systolic blood pressure to epinephrine and to methacholine (Mecholyl) has proved most useful. Funkenstein's original work demonstrated that patients showing a prolonged hypotensive effect with methacholine constitute the favorable cases for electroconvulsive therapy. The author's studies of 250 cases in office practice indicated that patients with an opposite reaction, i. e., those who overcompensate to methacholine, are favorable candidates for CO_2 narcosis therapy and for nonconvulsive electrostimulative treatment. Epinephrine-precipitated anxiety is also a favorable indication for the last two modalities, though unfavorable for ECT. Combining drugs like chlorpromazine with ECT may improve the response in patients falling into otherwise unfavorable autonomic groups for convulsive therapy.

The reactivity of the central sympathetic centers in the posterior hypothalamus appears to be of crucial importance. These centers are presumably underreactive in patients suitable for ECT and overreactive in those favorable for CO_2 and for nonconvulsive electrostimulation.

Future research may well be directed at finding even simpler tests, as well as investigating the reactions of the anterior hypothalamus to a test injection of arterenol.

Discussion

DR. ROBERT A. RICHARDS: A good start has been made in the attempt to correlate certain physiologic responses with the effects of certain specific treatments for psychiatric illness. On the other hand, these discoveries also raise many questions.

About three years ago, a procedure was set up at the Brentwood Veterans' Administration Hospital to make use of the methacholine test to study patients who were to receive electroshock treatment. It was discovered that these patients, who were for most part chronic schizophrenics, almost always were in Group I or Group II-III, with a correspondingly unfavorable prognosis with electroshock (approximately 30%). This constancy in chronic hospitalized patients limits the use of the test, as all we learn from the test is that only some 30% of this hospitalized group will respond to electroshock treatment. We do not know which patients comprise this 30%. At present, there is some danger in placing too much emphasis on the test findings. For example, a patient in Group I, which has a 10% favorable prognosis with electroshock, may not be given EST, although he may be the one in 10 who would respond. There is certainly need of some way by which to determine which of the patients in a specific grouping will respond and which will not.

In the course of a study of electroshock treatment at Brentwood VA Hospital, the patients were given serial methacholine tests, and it was noticed that the same patient fell in different groups on different days. Each test was given by a different student nurse. To study the reliability of the tests, a group of 14 chronic schizophrenic patients who would not be expected to change from day to day were given tests three times a week for one or two months. These tests were all administered by the same person. The patients all fell in Group I or Group II-III and, although they

showed occasional fluctuation between Group I and Group II-III, both with unfavorable prognosis, they very rarely fell into any other group. The test, therefore, appeared reliable. However, the changes noted when the test was given by different student nurses suggests that when serial tests are given, the same person should administer them.

Other studies at Brentwood may throw some light on the problem of why patients with the same type of response to methacholine respond differently to electroshock. Thus far, 60 patients have had numerous psychologic and physiologic tests, including methacholine tests, before and after electroshock. The data have not yet been analyzed. I hope that a survey of the correlations may reveal measurable differences in these patients, who now seem to fit into the same group but who have a different response to electroshock.

Report on European Psychiatry Based on Attendance at Five International Congresses and Visits to Scandinavia and Russia. Dr. Eugene Ziskind.

In various parts of the world psychiatry is given different emphases. This statement applies to the areas of unproved etiology and therapy, and not to those well established as specific or empirical. Hence, in Scandinavia certain conditions foster priorities in psychiatry for hereditary, epidemiologic, and follow-up studies; in mid-Europe, for existential philosophy; in Russia, for the psysiologic (Pavlovian) approach, and in the United States and England for (*a*) psychoanalysis and (*b*) interdisciplinary psychosocial collaborations.

These priorities for various trials and explorations in psychiatry in different world areas are much to the good. For where in the world will one find countries better adapted than the Scandinavian to carry on psychiatric hereditary studies, because, among other things, of their small, nonmigrant communities, "isolates," and excellent psychiatric registries; where a country more likely than Russia to pursue the Pavlovian investigations so intensively; where countries so wealthy as the United States and England, with so many persons who will support the long-term intensive psychoanalytic therapies? A tolerance for these various internationally emphasized "experiments of nature" in psychiatry is desirable, particularly in the absence of a better prevailing system, since the scientific method of objective demonstration will probably be the basis on which they gain universal acceptance or perish. Certainly, there were no significant delays in the scientific world for the acceptance of penicillin for the treatment of dementia paralytica or vitamin B_{12} for pellagrous psychosis once their effectiveness was demonstrated.

Status and other rewards accorded scientific careers in Russia were so noteworthy as to warrant emulation.

LOS ANGELES SOCIETY OF NEUROLOGY AND PSYCHIATRY

Regular Meeting, Nov. 20, 1957

Inflammatory Intervertebral Disk Disease as a Postoperative Complication of Surgery in the Lumbar Area. Dr. W. Eugene Stern.

A clinical and radiological study of nine patients was presented, each of whom had sustained lumbar disk herniation, confirmed at the time of operation. Each suffered a form of inflammatory or similarly progressive disease of the interspace and the adjacent vertebral bodies as a postoperative complication. There were three groups of patients: those in whom frank postoperative wound infection occurred; those in whom a sterile leptomeningeal reaction occurred, and those, comprising the largest group, had the inflammatory disk disease in the absence of any local wound suppuration. All patients experienced a continuation, recrudescence, or reappearance of lumbar pain, often with back spasms and regularly with limitation of back mobility. Systemic reactions were variable; the morbidity was prolonged and disabling, and the radiographic findings, which were often delayed in onset, consisted in areas of lysis, followed by loss of height of the interspace and sclerosis and collapse in the vertical dimension of the adjacent vertebral bodies adjoining the diseased disk area. The common process in all cases was inflammatory, in the sense of reaction to injury of low to moderate intensity, and of long duration, characterized by necrosis followed by proliferation of new tissue and calcification. The etiology of the process would appear to be bacterial in most, although it is suggested that other etiologic factors be given consideration in the pathogenesis, namely, an aseptic, nonbacterial process related to the primary degenerative disease responsible for the initial disk herniation.

Lysis of Lissauer's Tract. Dr. Robert W. Rand.

The potentiality of segmental destruction of Lissauer's tract and the associated lateral aspect of the posterior gray column for the control of root, lumbosacral, or brachial plexus neuralgia, due to an organic disease, has, up to the present

time, not been fully explored. In 1942 and 1943 Hyndman and associates demonstrated that sharply cutting the Lissauer tract in man in the thoracic region resulted in analgesia and thermanesthesia in a band three to five segments wide on the same side. In an effort to circumscribe the anatomical obstacle of the posterolateral arteries and their branches, the technique of controlled low-amperage, unipolar and bipolar electrolysis of the dorsolateral tract and underlying posterior gray matter has been undertaken in a series of cat and monkey experiments. Using the unipolar technique, peculiar patterns of infarction within the cord have been seen in about 50% of the experiments. Such areas of myelomalacia have not particularly been evident using the bipolar technique, which gives a more discrete longitudinal type of lesion. In cats and monkeys varying degrees of hypalgesia have been obtained after the making of such lesions, without other permanent adverse side-effects. These experiments are being carried out in the hope of standardizing the technique to a point of applying the operation to patients who are suffering from intractable organic pain of the brachial plexus, due to such lesions as apical carcinomas of the lung.

Radioisotopic Measurement of Cerebral Blood Flow. DR. PAUL H. CRANDALL.

Preliminary observations are presented, using a new radioisotope measurement of carotid-torcular blood flow on 17 patients with various clinical diagnoses. The method consists of the injection of 10μc. to 20μc. of radioactive iodinated (I^{131}) serum albumin into the common carotid artery and making a record by an external counting technique at the torcular Herophili. The torcular Herophili is located by an external scalp maker, which is related to the demonstration of the torcular on a contrast angiogram. A portable well-shielded scintillation counter is then placed 3 cm. above the lower edge of the torcular Herophili on the skull and at an angle of 30 degrees with a plane parallel to the Frankfort horizontal plane. After injection, a five-minute equilibrium count is made, and a blood sample for determination of total blood volume is taken.

We believe that the torcular Herophili blood flow during and immediately after injection is represented almost in isolation in the count rate because of its large size and close proximity to the scintillation counter. From the character of the curve obtained, it is possible to see a small rise, due to flow through the carotid and arterial system; a fall to near normal, and then a large parabolic curve, which can be attributed to the torcular blood flow. Circulation time is measured from the beginning of injection to the peak of the torcular curve and measured from 5.2 to 6.8 seconds, with the exception of several cases whose clinical diagnoses would indicate that a prolongation of the circulation time was consistent with the disease process. Volumetric measurement of blood flow through the torcular is accomplished when the total blood volume is known and the total count of the curve and an equilibrium value are obtained. It is necessary to resort to measurements in phantoms to obtain a corrected equilibrium value. Volumetric flow through the torcular measured from 250 to 350 cc. per minute in all patients.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY, AND NEW YORK NEUROLOGICAL SOCIETY

Joint Meeting, May 14, 1957

John McDowell McKinney, M.D., Chairman, Section of Neurology and Psychiatry, Presiding

RESIDENTS' PROGRAM

Inhibition by Chlorpromazine of the Adrenocortical Response to Insulin Stress in Man. DR. MARY KNIGHT, DR. NICHOLAS P. CHRISTY, DR. WILLIAM A. HORWITZ, and DR. DONALD LONGSON, New York State Psychiatric Institute.

Nine schizophrenic patients undergoing therapeutic insulin coma were given 100 to 300 mg. of chlorpromazine orally before their insulin injections. The plasma corticosteroid levels were studied before insulin and at three and four hours after insulin and were compared with plasma corticosteroid levels of the same insulin coma subjects without chlorpromazine. Although chlorpromazine was found to interfere slightly with the Silber-Porter method of determining plasma corticosteroids, there was a significant difference between the levels with and without chlorpromazine premedication, the usual rise after insulin administration being inhibited by the drug. This was confirmed by paper chromatography.

Long- and short-term administration of chlorpromazine did not inhibit the response of the adrenal cortex to exogenous corticotropin.

A complete report is given in the *Journal of Clinical Investigation* (36:543, 1957).

A New Diagnostic Technique for Demonstrating Tumors of the Posterior Fossa by the Use of Iophendylate (Pantopaque). Dr. David R. Cobbon, Mount Sinai Hospital.

A preliminary report is made of the techniques and results of a contrast medium technique for demonstrating mass lesions of the posterior fossa as filling defects by the use of iophendylate. The procedure is called "Fossagraphy" or "Pontography." Iophendylate, in the amount of 15 to 18 cc., is injected in the manner usual for myelography, and, by various maneuvers, the contrast medium is pooled within the posterior fossa to outline its anatomic configuration. X-rays in the posteroanterior, lateral, and left and right oblique views are taken.

In the present report this procedure was performed in 12 cases in which the possibility of a posterior-fossa neoplasm was included in the differential diagnosis. In three patients with a filling defect, a tumor was verified by surgery. Although variable amounts of iophendylate were spilled above the tentorium, there were no untoward reactions, except a transient meningismus in one patient.

A posterior-fossa air study was not helpful in two of the cases in which there was an abnormal fossagram corresponding to a surgically proved lesion.

On the basis of these data, it is concluded that this technique is capable of yielding diagnostically useful information. The most serious limiting factor is that of supratentorial spillage, which may represent more of a medical-legal than a real clinical problem.

Angiographic Demonstration of Collateral Circulation in the Cerebrum in Vascular Occlusions. Dr. Gerard M. Lehrer, Mount Sinai Hospital.

During the course of routine cerebral arteriography done at the Mount Sinai Hospital over the course of the past three years, 18 patients were found in whom major occlusions of the cerebral blood supply were demonstrated. Of 13 patients who showed thrombosis of one internal carotid artery, collateral arterial supply could be clearly demonstrated in 9. In eight of the latter, shunts were shown between the external and the internal carotid circulation via the ophthalmic artery and its branches, and in one, between the vertebral and the carotid circulation via the posterior communicating artery. Retrograde filling of the major branches of the middle cerebral artery by way of anastomoses with the anterior cerebral artery on the surface of the brain could be demonstrated in three out of five patients with middle cerebral artery occlusion. Three cases are presented in detail. Although the clinical pictures appear to indicate that these collateral pathways form an important contribution to the cerebral blood supply in some of the cases presented, a review of the total clinical data reveals no correlation between age, mode of onset, or severity of symptoms and course and the arteriographic demonstrability of collateral blood supply by unilateral arteriography. The need for further study of clinicoradiographic correlations with complete cerebral angiography in patients with occlusive cerebrovascular disease is emphasized.

Effect of CO_2 on Steady Cortical Potential in Dogs. Dr. Robert Katzman and Dr. Eli S. Goldensohn, Department of Neurology, Columbia University College of Physicians and Surgeons, and the Neurological Institute, Presbyterian Hospital.

Direct-current or steady potentials were measured in the cerebral hemispheres of 37 dogs. Initial operative procedures were performed under thiopental (Pentothal) and local procaine anesthesia, the animals being maintained on succinylcholine with artificial respiration.

The steady potentials were measured with silver-silver chloride electrodes rigidly mounted in glass jackets and connected to the tissue with isotonic saline bridges. The potentials were amplified by a Grass chopper-type converter-demodulator and recorded with an ink writer.

In the resting cortex there is a potential gradient such that the sigmoid gyrus is 1.4 ± 0.3 mv. positive to the suprasylvian gyrus. The cortex at the suprasylvian gyrus is 1.2 ± 0.4 mv. positive to an electrode connected to the subcortical white matter or ventricle.

When the animal breathes a mixture of 80% oxygen and 20% CO_2, these resting potential gradients change, the suprasylvian gyrus becoming 1.4 ± 0.1 mv. positive to the sigmoid gyrus and the white matter becoming 2.6 ± 0.1 mv. positive to the cortex. This response closely parallels the pH shift of the cortex, as measured by a glass-membrane pH electrode set on the pia adjacent to the D. C. electrode.

Intravenous infusions of 5% sodium bicarbonate produce a shift in the steady potential opposite that produced by CO_2, whereas intravenous acids produce a shift in the same direction as that produced by CO_2, but irregular in form. Locally applied phosphate buffers (pH 6.5 to 7.5) and locally applied bicarbonate solutions do not change the steady potentials.

It is concluded that lowering the cortical pH increases the positivity of the subcortex relative

to the cortex and of the sigmoid gyrus relative to the suprasylvian gyrus.

These results cannot be explained on the basis of the known hyperpolarizing effect of CO_2 on resting membrane potentials unless it be postulated that greater hyperpolarization occurs in deep structures than in superficial gray matter.

A Systematic Review of Intracranial Aneurysms at the Presbyterian Hospital, New York, from 1914 to 1956. DR. EDGAR M. HOUSEPIAN, Neurological Institute.

A review of 113 cases of pathologically verified aneurysm is presented. This represents the entire number of intracranial aneurysms found in over 13,000 autopsies at the Columbia-Presbyterian Medical Center over the 41-year period from 1914 to 1956.

The difficulties in formulating a useful classification because of inconclusive evidence concerning the role of arteriosclerosis in the genesis of certain intracranial aneurysms are discussed. It is shown that arteriosclerosis favorably influences the prognosis.

Observations regarding the age and population incidence, frequency, and types of hemorrhage of the various morphologic types of intracranial aneurysm in different locations are presented.

Conclusions are drawn suggesting that the prognosis for untreated, symptomatic intracranial aneurysms is grave, 61% of such patients having died within four weeks following the onset of their initial symptoms.

It is conceded that a study based on autopsy statistics is biased, but that this information is so strongly suggestive that substantiation by a long-term, careful study of clinically verified cases is imperative. The results of surgical therapy cannot be rationally evaluated until this is done.

Finally, it is noted that without a combination of efforts to pool systematized information regarding autopsy-verified cases of intracranial aneurysms, one could not accumulate a statistically significant number of cases from a single hospital in a lifetime.

Discussion

DR. MORRIS B. BENDER: I do not believe that mortality statistics are of practical aid in the evaluation of patients in the clinic.

A Study of Alcoholism with Onset at Age of Forty-Five or Older. DR. HARRY H. MOORHEAD, New York Hospital-Westchester Division, White Plains, N. Y.

A study was made of 61 cases in which alcohol became a problem at the age of 45 or older. A statistical review of hereditary and environmental factors was presented. Results of follow-up studies after hospitalization were reported, indicating that 11, or 18%, of the patients became abstinent, and 16, or 26%, managed better, for a total of 44% who were definitely benefited. The average age of the abstinent group at the time of hospitalization was 56, and the span of follow-up was from 2 to 12.5 years, with an average duration for follow-up of 6.2 years. The abstinent group showed better personality organization, less rigidity, and more energy, and, as a result, were better able to manage the stress factors in the environment which contributed to their problem. The study suggested that alcoholism is as malignant a disorder in the older age group as in the younger. The personality inadequacies and the external stress were essentially similar in older alcoholics as in younger alcoholics, except that in the former the stress manifested itself differently, as would be expected in persons of middle or older age.

Leptomeningeal Carcinomatosis: Report of Case. DR. HERBERT BENGELSDORF and DR. ROSA FIOL, Neurology Section and Pathology Department, Veterans' Administration Hospital, Bronx, N. Y.

A 55-year-old man was admitted to the hospital in January, 1955, complaining of paralysis of the right side of his face and deafness for the past few months. Examination revealed a right peripheral facial palsy, bilateral perception deafness, and nonfunctioning labyrinths. His course was slowly but relentlessly downhill, with the appearance of left facial palsy, hypalgesia of the snout area of the face, dysphagia, dysphonia, atrophy, weakness and sensory loss in a radicular distribution involving chiefly the lower extremities, bilateral Babinski sign and loss of superficial abdominal reflexes, and urinary incontinence. He became emaciated and bedridden, but remained alert and responsive until he died in July, 1956, or 22 months after the onset of symptoms.

The spinal fluid showed consistently moderately elevated protein values, usually less than 100 mg.% and up to 50 lymphocytes per cubic millimeter. The sugar content was within normal limits until terminally, when it fell to 36 mg.%.

At autopsy a microscopic alveolar-cell carcinoma was discovered with tumor cells within the lumina of the surrounding blood vessels. There were no metastases, except to the leptomeninges. Grossly there was thickening of the meninges of the spinal cord, with no macroscopic evidence of tumor. The subarachnoid space overlying the cerebellum, brain stem, and spinal cord was lined with the carcinoma cells, which extended along the nerve roots of the cauda equina and into the perivascular spaces. Myelin-sheath stains of spinal cord sections showed extensive, diffuse degeneration, chiefly in the posterior columns, but no tumor cells were

found within the parenchyma of the brain, spinal cord, or nerve roots.

Attention is called to the unusually long duration of illness, the absence of meningeal signs, and the inability to demonstrate tumor cells or a depression of sugar content in the spinal fluid.

Reevaluation of Lumbar Puncture in Presence of Papilledema and Intracranial Hypertension: A Study of 129 Cases. Dr. Julius Korein, Dr. Mario Leicach, and Dr. Humberto Cravioto, Department of Neurology, Third Division, New York University-Bellevue Medical Center.

This study was undertaken in an attempt to reevaluate the problems concerning the advantages and complications of lumbar puncture in conditions causing intracranial hypertension. Although it is widely held that lumbar puncture is contraindicated in patients with increased intracranial pressure and/or papilledema, there is much controversy regarding this opinion. Recent reports suggest that the dangers have been overemphasized, and the authors believe it important to present their own experiences.

The material, from Bellevue Medical Center, includes 70 cases with papilledema and 59 cases without papilledema, but with increased cerebrospinal fluid pressure. All had lumbar punctures prior to any surgery. Approximately 50% of the cases with papilledema had intracranial neoplasms (five in the posterior fossa), while only 25% of the cases with increased cerebrospinal pressure without papilledema had neoplasms (four in the posterior fossa).

Possible complications were recorded as any unfavorable change of state within 48 hours after lumbar puncture. One possible complication occurred in the group with papilledema (1.4%) and seven possible complications occurred in the nonpapilledema group (12%). On reviewing these possible complications, it seems doubtful whether any can be said to be causally related to the lumbar puncture.

The one patient with papilledema and two with increased pressure had intracranial hemorrhage and died soon after admission and lumbar puncture. Two tumor cases and one with a bilateral subdural hematoma had episodes of transient or deepening lethargy within 48 hours after lumbar puncture. In one patient with advanced tuberculosis and anemia, who had a grand mal seizure, two lumbar punctures were performed after the patient went into coma, and she died within 24 hours. Autopsy in this last case showed no significant central nervous system pathology. It is difficult to attribute these changes to the procedure, since there are many patients with similar lesions who had no lumbar puncture and still had similar changes of state.

Over 45% of the patients with papilledema had non-neoplastic lesions, and in many of these cases lumbar puncture was essential to the diagnosis. Furthermore, the puncture in many of these cases gave enough diagnostic information to obviate surgical procedures, such as ventriculography, which would not have benefited many of these patients.

From this study and a review of similar studies from the literature, one can say that careful lumbar puncture in the presence of papilledema is significantly less dangerous than is generally believed, and the use of lumbar puncture in diagnosis and treatment is of great value and often prevents unnecessary surgery. We conclude, therefore, that papilledema is not a contraindication to careful lumbar puncture.

Discussion

Dr. J. Lawrence Pool: Lumbar puncture, including pneumoencephalography, in the presence of increased intracranial pressure can be dangerous, especially in cases of temporal lobe or posterior-fossa tumors when uncal or tonsillar herniation is already a threat. For such cases, in particular, I feel, with other neurosurgeons, that lumbar punctures should not be done.

Dr. Morris B. Bender: The neurosurgeon constantly reiterates that lumbar puncture is dangerous in the presence of increased intracranial pressure. I was never convinced of this, and the facts presented today by Dr. Korein support my contention. I am sure there are some people with increased intracranial pressure who die after a lumbar puncture, but many of these patients are so dangerously ill that death may occur even without a spinal tap. I have had several patients with brain tumor who died suddenly without lumbar puncture. In fact, more patients die without lumbar puncture than with it. Spinal tap is important because it gives us valuable information, and I think it should be done in almost every case with a neurologic problem.

NEW YORK NEUROLOGICAL SOCIETY

Irving J. Sands, M.D., President, Presiding

Regular Meeting, Oct. 2, 1957

Presidential Address: The Neuropsychiatric Aspects of Juvenile Delinquency. Dr. Irving J. Sands, Brooklyn.

Brain Tumors Masked as Parkinsonism. Dr. Murray E. Margulies.

A complete Parkinsonian syndrome, or fragments of one, may be caused by brain tumors.

Case 1.—A white, right-handed woman, aged 55, developed stiffness involving the left lower extremity and, later, the left upper extremity. The first diagnosis was Parkinsonism. Weakness progressed rapidly; a Babinski toe sign developed. At craniotomy an infiltrating tumor involving the right frontal lobe was encountered.

Case 2.—A white, right-handed man first noted tremor at rest involving the left upper extremity. Two physicians made the diagnosis of Parkinsonism. Pneumoencephalography revealed a shift of the ventricular system to the left side. At operation a meningioma of the sphenoid ridge was removed.

Case 3.—A 68-year-old, right-handed man complained of headaches in 1945 and later stiffness of the hands and feet. The first diagnosis was hypertension; later it was changed to arteriosclerotic vascular disease and Parkinsonism. Because of a bilateral Babinski toe sign and aphasia, pneumoencephalography was done. At craniotomy a meningioma of the sphenoid ridge on the left side was removed. Careful follow-up observation for the past six years has shown no reappearance of his signs and symptoms of Parkinsonism.

This paper is presented to emphasize that at times brain tumors produce a picture of Parkinsonism, which cannot be diagnosed without pneumoencephalography and/or cerebral angiography. The mechanism producing Parkinsonism in cases with space-occupying, expanding lesions which do not directly invade the structures of the extrapyramidal motor system remains obscure. Does the frontal pole exert a dynamic influence on the basal ganglia through their connections, as first suggested by Ludo van Bogaert, or is the physiologic derangement the result of the disturbance of circulation?

Pathophysiologic Evolution of Amaurotic Familial Idiocy. Dr. Stanley M. Aronson, Dr. Abraham Saifer, and Dr. Bruno W. Volk, Brooklyn.

Serial clinical, pneumoencephalographic, biochemical, and pathologic data derived from 73 cases of infantile amaurotic familial idiocy were reviewed. On the basis of the findings, it was found convenient to divide the disorder into three phases. The first phase, corresponding to the first 14 months of illness, was characterized by diffuse intracerebral atrophy and markedly elevated serum and spinal fluid glutamic-oxalacetic transaminase. The second phase, representing the disease up to 24 months, was characterized by a rapidly developing megalencephaly, confirmed radiographically, cephalometrically, and pathologically. The serum aldolase was elevated, presumably due to the coincident muscle atrophy. The third phase (over 24 months of determined illness) showed an accentuation of the previous findings except for normal aldolase levels. Biochemical changes relating to serum protein fractionation and serum neuraminic acid were also described.

The serum enzymatic alterations considered typical of amaurotic familial idiocy have been noted in a clinically healthy infant who subsequently developed the classic symptomatology of the disorder. It would therefore appear feasible to establish the diagnosis of amaurotic familial idiocy by serologic procedures, possibly even prior to the emergence of the pathognomonic diagnostic signs.

Discussion

Dr. Louis Obessky, Brooklyn: I would like to ask Dr. Aronson two questions. First, in the photographs he showed that there was a widening of the sulci and that there was air in those spaces. Where did the air come from? Second, was any determination of cholesterol and lipids done on the serum?

Dr. Stanley M. Aronson: Insofar as the first question is concerned, these photographs represent pneumoencephalograms, and the air is the consequence of introduction of air into the subarachnoid spaces.

In reply to the second question, Dr. Saifer has done exhaustive studies not only on cholesterol but on a wide variety of lipid fractions, and, although there are some changes, these are of such slight degree that we would prefer to attribute them to nonspecific causes rather than to any reflection of the disease itself.

Dr. Jeanne Smith: How many of the families in which these children occur have siblings which are normal?

Dr. Stanley M. Aronson: We have accumulated a considerable body of genetic data, unfor-

found within the parenchyma of the brain, spinal cord, or nerve roots.

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tunately not as yet completely evaluated from a statistical point of view. It would be pointless to take any family which has had only one child, and most of our cases fall in that category. We have advised parents, when the first child with Tay-Sachs disease appears, not to have more children. We have had braver parents who have gone on, for whatever personal reasons motivated them, and we have genealogies on many of these families. Approximately one-fourth of any aggregate sibling group will come down with the disease. Unfortunately, we know of several families in which four consecutive children have come down with the disease; contrariwise, we have one family with six children; only one has shown the disease.

Factors Contributing to Failure in Surgery of the Low-Back Syndrome. Dr. Edward B. Schlesinger.

This paper analyzed the causes of failure of the disk-and-fusion procedure in 38 cases, totaling 197 years of disability and various degrees of drug addiction. Only technical factors were emphasized, including anatomic variants, such as narrow interpediculate measurements and the less common narrow anteroposterior diameter. A large number of cases on repeat myelography showed traumatic meningoceles and severe cicatrix formation. This was considered to be due largely to difficulty in exploration because of excessive bleeding. Slides were shown illustrating the dramatic changes in venous pressure within the extradural circulation in patients lying in the prone position when the abdomen is compressed and when anesthesia complications occur. Vascular occlusion marked as disk disease was also described and illustrated. The significance of cephalad progression of the fulcrum of motion of the low back following fusion was emphasized, with illustrations of the degenerative changes occurring at the next higher interspace. The importance of this concept in terms of future outlook cannot be overemphasized and deserves further careful study.

Discussion

Dr. Theodore R. Robie, East Orange, N. J.: It should be said that one must have great admiration for a surgeon that has the backbone to make a report of this kind. We usually are treated only to the *good* results. I think every one of us should take his hat off to Dr. Schlesinger.

Abstracts from Current Literature

Edited by Bernard J. Alpers, M.D.

Psychiatry and Psychopathology

Senility—Its Nature, with Some Thoughts Concerning Treatment and Prevention. Charles D. Aring, A.M.A. Arch. Int. Med. 100:519 (Oct.) 1957.

Aring regards senility as a decompensatory behavioral stereotype acquired partially at least through psychological conditioning stemming from certain cultural tendencies in contemporary Western civilization. The critical factors would seem to be social and emotional isolation, sensory deprivation, and monotony. Although physical factors, especially results of impairment of blood supply to brain-stem reticular activating centers and cortex due to atherosclerosis, vasospasm, thrombosis, cervical hyperostosis, absence of functional anastomoses and impairment of the general circulation may form the pathophysiologic substratum for the clinical picture observed, treatment of these factors is frequently ineffectual. Rehabilitation consequently must be oriented toward psychological approaches, such as environmental modification designed to supply the challenge and variety of stimulus usually missing from the lives of these patients. Institutionalization should be deferred as long as practicable. Prophylaxis is largely a matter of cultivating the proper breadth and depth of emotional and intellectual interests, while avoiding habits of restriction and isolation in the years prior to the senium.

Parsons, Montrose, N. Y.

Meninges and Blood Vessels

Proteus Meningitis: Report of a Case in a Newborn Caused by Proteus Mirabilis. H. C. Tolmas and J. Winter, A.M.A. J. Dis. Child. 94:574 (Nov.) 1957.

Proteus meningitis is a rare entity, and that due to Proteus mirabilis, presumably a common inhabitant of the intestinal tract, is unique.

Tolmas and Winter report on a 4-day-old infant who, after a normal delivery and neonatal life, became irritable and developed fever. No other abnormalities were observed. The spinal fluid was cloudy and contained 8400 leukocytes per cubic millimeter, with 89% polymorphonuclear cells and 11% lymphocytes; protein measured 210 mg. %, chlorides 726 mg. %, and glucose 41 mg. %; many Gram-negative pleomorphic bacilli were seen on smear. Cultures of blood and spinal fluid revealed P. mirabilis. The organism was sensitive to neomycin, dihydrostreptomycin, and novobiocin (Albamycin), the last two of which were administered. Bilateral catarrhal otitis media became manifest three days after onset and was presumed to have been due to the septicemia. The response to treatment was good, and after two weeks the infant was well. The organism was found in the mother's stool.

Siekert, Rochester, Minn.

Diseases of the Brain

The Clinical Aspects of Cerebral Vascular Insufficiency. E. Corday and S. F. Rothenberg, Ann. Int. Med. 47:626 (Oct.) 1957.

The authors discuss the factors which produce transient episodes of cerebral symptoms, either focal or generalized, and thought to be on a vascular basis.

Angiospasm of the cerebral vessels is dismissed after a review of Pickering's work, in 1948 and 1951, that of Walker, in 1953, and Forbes, in 1933. The authors' attitude toward angiospasm is emphasized by their previous experiments with rhesus monkeys, in which it was demonstrated that the pial vessels did not change caliber under direct mechanical, thermal, or adrenal stimulation and that only a drop in systemic blood pressure could cause significant pial arterial narrowing.

The authors' concept of cerebral vascular insufficiency is proposed as the possible etiology of "little strokes." This concept was originated in 1953 and is defined physiologically as a deficiency of the cerebral arterial blood flow resulting from an inadequate systemic arterial

blood pressure or impairment of the cardiac output, usually in the presence of narrowed cerebral vessels. If generalized, syncope, generalized seizures, etc., may be the result. If focal, hemiplegia, sensory disturbances, Jacksonian seizures, etc., may occur. The common denominator is a diminution in the intracerebral blood pressure.

This concept is further strengthened by the appearance of transient electroencephalographic abnormalities which occurred with systemic hypotension produced by clamping the carotid and vertebral arteries on one side. These were reversible with the restoration of the normal blood pressure.

The authors list 22 clinical conditions in which cerebral vascular insufficiency may occur. These are hemorrhagic, coronary, anaphylactic, insulin, and traumatic shock; antihypertensive drugs; postsympathectomy; hypersensitive carotid sinus; postural hypotension; hypotensive episodes of reflex origin; cardiac arrythmias; surgical procedures; anesthetics; congestive heart failure; pulmonary hypertension; thermal vasodilatation; Valsalva maneuver; gravitational states; angiography; hypothermia; sleep, and pulmonary embolism.

AIGNER, Rochester, Minn.

GENERALIZED TETANUS: ANALYSIS OF 202 CASES. M. R. GARCIA-PALMIERI and R. RAMIREZ, Ann. Int. Med. 47:721 (Oct.) 1957.

The authors present a summary of 202 cases of tetanus seen from 1940 to 1955. The ages of the group varied from 12 to 84 years. The disease was three times as common in males as in females. No significant difference was found in the mortality rate in cases with the portal of entry in the head and neck and those with the portal of entry in the lower extremities. It was found that those patients with a shorter incubation period (10 days or less) had a higher mortality rate than those with a longer history of the disease.

In general, the main symptoms in tetanus are referable to the neuromuscular system. Trismus (171), convulsions (75), dysphagia (64), back pain (59), and stiff neck and abdomen (53) were the commonest complaints. The mortality rate of those with convulsions was two and a half times that of patients without seizures. The most striking signs also were the result of secondary changes due to increased activity of the neuromuscular system. Trismus (196), fever (173), abdominal rigidity (168), hyperactive deep reflexes (137), nuchal rigidity (137), convulsions (118), opisthotonos (95) were the commonest. The higher the temperature, the poorer was the prognosis.

Therapy consisted of tetanus antitoxin after skin testing. Doses of 20,000 to 100,000 units were given initially intramuscularly, and doses of 20,000 to 100,000 units were given intravenously in 300-1000 cc. of saline or a 5% dextrose solution. Further doses, from 20,000 to 80,000 units a day in divided or single doses, were given for 3 to 12 days. Best results were obtained in those patients who received 30,000 to 60,000 units intramuscularly and 40,000 to 60,000 units intravenously initially, followed by 10,000 to 20,000 units two times a day for three to five days.

Local debridement was carried out, and parenteral phenobarbital sodium and penicillin were also administered.

Of the 202 patients, 66 died, a mortality of 32%. The most frequent cause of death was respiratory failure.

Six patients developed the disease despite the prophylactic administration of 1500 units of tetanus antitoxin the day of the original injury.

An episode of the disease does not confer permanent immunity. Five recurrent cases were found in this series.

AIGNER, Rochester, Minn.

MUSICOGENIC EPILEPSY: REPORT OF 3 CASES. D. D. DALY and M. J. BARRY JR., Psychosom. Med. 19:399 (Sept.-Oct.) 1957.

Sporadic convulsions initiated by variable sensory stimuli are referred to as reflex epilepsy. Seizures induced when the patient is listening to music are called "musicogenic epilepsy."

After a review of a number of the 30 cases reported thus far in the literature, the authors report 3 cases of their own which fall into this category. Spells were found to be brought out by various musical stimuli. Some patients had spells with any type of music; one patient had an attack when listening to a monotonous lecture; another, after sawing wood; in others thinking out a tune produced a seizure, while in yet others hearing music was not sufficient unless it was actually listened to.

The authors' first case of seizures defined as primary musicogenic epilepsy is that of a 24-year-old woman who had psychomotor and generalized motor seizures upon listening to swing or jazz music. These were reproduced by playing "String of Pearls" during an electroencephalogram examination. The tracing showed a brief generalized discharge of 5-6 per second waves, not reproducible by other stimuli. Psychotherapy over a prolonged time brought about marked improvement. Two other cases of secondary musicogenic epilepsy are also presented. The authors separate primary from secondary types, including in the former attacks which bear an intimate relationship to music and in the latter seizures which occur independently of music, particularly those attacks which later come to be precipitated by music. In the latter group an underlying convulsive disorder exists, and the authors present an interesting commentary on the effectiveness of simple auditory patterns in triggering this phenomenon.

AIGNER, Rochester, Minn.

CEREBRAL INFARCTION SIMULATING BRAIN TUMOR. E. H. WOOD and T. W. FARMER, Radiology *69*:693 (Nov.) 1957.

Occlusion of the internal carotid artery or the middle cerebral artery causes unilateral cerebral edema on the affected side. This unilateral cerebral edema often produces contralateral displacement of the intracranial structures, including the pineal gland and the ventricular system. Displacement of these structures away from the midline, when combined with symptoms of intracranial disease, can sometimes lead to the diagnosis of a brain tumor or some other expanding intracranial lesion.

Wood and Farmer give case histories of four patients with cerebral thrombosis in whom displacement of the intracranial structures was demonstrated radiologically or pathologically. Findings in four cases described by other authors are tabulated. Wood and Farmer believe that carotid angiography will establish the correct diagnosis in this condition. Angiography is not without risk in patients with vascular disease, but the risk often is considerably less than the risk of craniotomy.

WEILAND, Grove City, Pa.

SUDDEN LOSS OF MEMORY. ALEXANDER KENNEDY and JOSEPH NEVILLE, Brit. M. J. *2*:428 (Aug. 24) 1957.

The etiology of sudden loss of memory was investigated by Kennedy and Neville in two series of cases. In all, 74 patients were subjected to complete neurologic and psychiatric examinations. A large proportion of patients in both series suffered from undetected gross organic nervous disease. In the majority, the amnesia could be demonstrated to be a psychologic escape mechanism. The authors state that there is evidence that organic nervous disease may predispose to this type of psychologic mechanism. Sudden amnesia is a temporary state that responds well to simple psychotherapy. The authors point out the importance of seeking the causes of the patient's underlying maladjustment not only in his life and circumstances but in his central nervous system as well.

ECHOLS, New Orleans.

HYPERTENSIVE CEREBRAL SCALARIFORM ARTERIOSCLEROSIS. ANTOINE ARAB, Psychiat. et neurol. 134-175 (Sept.-Oct.) 1957.

Scalariform arteriosclerosis is a condition wherein cholesterol granulomas of the media assume the form of yellow linear spirals, involving mainly the elements of the circle of Willis. It is rather rare and usually affects patients with arterial hypertension. Arab reviews a group of 69 cases in which necropsy studies established the diagnosis. Clinical symptoms developed over a wide range of years, with predominance between the age of 50 and 75. Death occurred at the age of 55 to 85, and correlation with onset of symptoms was achieved with difficulty, except in cases of younger men, among whom were included several instances of death in the fourth and fifth decades. The average duration of the symptoms varied from 1 to 12 years, with the majority under 8 years. Symptoms were of a sudden focal neurologic nature in 44 patients; 87% showed vascular retinopathy, and 80% evidenced significant arterial hypertension. At necropsy adrenal cortical hyperplasia was encountered in a statistically significant group, and this is regarded as a manifestation of the adaptation syndrome.

PARSONS, Montrose, N. Y.

Bilateral Optic Nerve Glioma with Misleading Encephalogram. Catherine Haberland, Psychiat. et neurol. 134:215 (Sept.-Oct.) 1957.

Haberland reports the case of an 11-year-old girl with a history of loss of visual acuity, of several weeks' duration, with exophthalmos and ptosis, right papilledema and left optic atrophy, pubertas praecox, and café au lait spots on the skin. The presumptive diagnosis of frontal brain tumor was made, and air studies revealed symmetrical dilatation of the lateral ventricles with filling defect of the third ventricle, suggesting tumor of the third ventricle. Craniotomy disclosed merely attenuation of the left optic nerve. The patient died six days postoperatively, and autopsy revealed a gliomatous tumor of the intraorbital portion of both optic nerves. Partial coalescence of the dorsal portion of the thalamus was noted. The authors point out the confusion with the third-ventricle tumor arising from the thalamic anomaly. The presence of skin lesions suggestive of von Reckinghausen's neurofibromatosis, in which disease bilateral optic nerve glioma may occasionally be seen, is cited as a further aid in diagnosis.

Parsons, Montrose, N. Y.

Changes of the Blood Pressure Produced by Intracranial Tumours. C. Arseni, I. Opresc u, and D. C. Samitca. Psychiat. et neurol. 134:230 (Sept.-Oct.) 1957.

The authors cite 11 cases of patients with brain tumor in whom changes of blood pressure were considered pertinent to the presence of the tumor. In most of these instances there was paroxysmal elevation of blood pressure, which subsided after removal of the tumor. The tumors included four involving the convexity of the frontal lobe, one temporal-lobe tumor, one third-ventricle papilloma, two cerebellopontine angle tumors and two pontine gliomas. The authors hypothesize three sites wherein there is experimental evidence of alterations of blood pressure following stimulation: the orbitofrontal gyrus and cingulus areas, the sensorimotor cortex, and the anterior temporal and insular regions. The transmission of pressor effects occurs by way of brain-stem pathways, some of which stem from hypothalamic relay pathways, notably the dorsal longitudinal bundle of Schutz. Lesions impinging upon the hypothalamus may exert pressor effects through the production of hormonal effects by way of hypothalamic-hypophyseal-adrenal relationships. The implication of descending pathways serves as a convenient explanation of the arterial hypertension frequently noted in posterior-fossa lesions.

Parsons, Montrose, N. Y.

Diseases of the Spinal Cord

Arachnoidal Cholesteatomas as a Late Complication of Intrathecal Injections for Tuberculous Meningitis of Childhood. D. Oeconomos and A. Caracalos, Rev. neurol. 97:81 (Aug.) 1957.

The authors have observed 10 cases of arachnoidal cholesteatoma in children treated for tuberculous meningitis 3 to 10 years previously by intrathecal injection of streptomycin. The symptoms developed insidiously and consisted of backache and root pains, and there were signs of spinal cord compression or involvement of the cauda equina. Of the 10 cases, 4 had normal spinal fluid findings. Myelography gave evidence of block, fragmentation, or defects in the column of the radiopaque material. Nine subjects had the mass at the site of the lumbar puncture; one subject had the mass at T_{8} and another at T_{10}. They were most frequently attached to a single root, where the arachnoid was thick and vascular. There was a capsule which was thickest at the point of attachment, and in the interior there were concentric layers of cholesterol.

Berlin, New York.

Peripheral and Cranial Nerves

Facial Palsy. T. Cawthorne and D. R. Haynes, Brit. M. J. 2:1197 (Nov. 24) 1957.

Cawthorne and Haynes attribute the frequency of facial palsy to the fact that the course of the facial nerve is long and tortuous through a small bony canal in the temporal bone. They made a study of 557 cases of facial palsy encountered during the past few years at several hospitals in London. Of the cases of facial palsy, 62% were due to Bell's palsy, 15% to injury, 7% to a lesion at the geniculate ganglion, and the remainder to infection, neoplasm, spasm, nuclear lesions, or birth injury. Bell's palsy is believed to be due to ischemia, result-

ing from swelling of a segment of nerve or its covering in the bony canal. Differentiation of lesions near the stylomastoid foramen, at the geniculate ganglion, and in the nucleus can often be made by testing the ability to taste and to lacrimate in a patient with facial palsy.

The authors state that "the only alternative to leaving things to nature" is surgical exposure of the nerve trunk at the site of the lesion. Results of exposing the facial nerve trunk at the site of the lesion in 196 cases were good in 136, fair in 46, and poor in 14. For facial palsy that is slow to recover or in which surgical treatment is contraindicated, they suggest use of an intraoral splint to reduce the deformity from a drooping mouth and vigorous manipulation of the face with grease-covered fingers three or four times a day. If all other treatment proves unsuccessful, faciohypoglossal anastomosis or a facial sling procedure may be tried.

ECHOLS, New Orleans.

Vegetative and Endocrine Systems

CUSHING'S SYNDROME IN INFANCY. R. E. GREENBLATT, J. M. MANAUTOU, A. M. ZIMMERMAN, and W. T. LUCAS, A. M. A. J. Dis. Child. 94:691 (Dec.) 1957.

Cushing's syndrome in children and infancy is extremely rare. The causes include carcinoma, hyperplasia and adenoma of the adrenal cortex, and pituitary adenoma.

Greenblatt and co-workers report on a 5-month-old girl with a benign adrenal cortical adenoma. Obesity, moon face, enlarged clitoris, and pubic hair were present. Faint calcification in the region of the tumor was seen on the abdominal roentgenogram. Urinary excretion of 17-ketosteroids was 6.5 mg. per 24 hours (normal, 1 mg.); 17-hydroxycorticoid excretion was 9.4 mg. per 24 hours (normal, 1-4 mg.). Injection of corticotropin did not influence these levels appreciably, suggesting a tumor rather than hyperplasia. Circulating eosinophils were absent.

Polydipsia, polyuria, alkaline urine, and high serum sodium (150 mEq. per liter) suggested an "aldosterone" component.

Corticoids and corticotropins were administered before, during, and for several weeks after operation, which was uneventful.

SIEKERT, Rochester, Minn.

Treatment, Neurosurgery

TREATMENT OF TUBERCULOUS MENINGITIS WITH A COMBINATION OF ISONICOTINIC ACID HYDRAZIDES, STREPTOMYCIN AND PARA-AMINOSALICYLIC ACID. E. APPELBAUM and C. ADLER, Ann. Int. Med. 47:782 (Oct.) 1957.

Appelbaum and Adler report the results of therapy in 41 cases of tuberculous meningitis with combined antituberculous medication. The ages of the patients varied from 7 months to 64 years, with a majority of patients in the first two decades. The duration of the meningeal involvement at the beginning of treatment varied from two days to two months, 22 cases being treated within two weeks of the onset. The diagnosis was confirmed bacteriologically in 26 cases by finding acid-fast bacilli in the cerebrospinal fluid by smear or culture or both.

The oral dosage of the hydrazides varied from 4 to 18 mg. per kilogram of body weight, 10 mg. per kilogram being most frequently used. The duration of this therapy varied from four months to four years four months.

Streptomycin was given intramuscularly in dosages of less than 1 to 2 gm. per day. The duration of treatment varied from 3 days to 17 months.

The aminosalicylic acid dose varied from 2 to 12 gm., given orally for one month to two years.

The initial changes indicative of clinical improvement following the combined therapy became apparent at varying intervals. Remission of fever was attained in 1 to 10 weeks. Improvement of the mental state and signs of meningeal irritation were noted in two to eight weeks. A state of well-being and gain in weight became manifest in a majority of the cases in one to three months. After the initial favorable response, improvement progressed slowly and was interrupted by occasional febrile episodes, and at times adverse developments, such as spasticity, paraplegia, hemiparesis, visual impairment, deafness, decubitus ulcers, and bladder calculi. Most of these complications cleared gradually, but some persisted.

The organisms disappeared from the spinal fluid early, and the return to normal of the other CSF abnormalities was delayed for weeks or months.

In 41 cases, there were 29 recoveries and 12 deaths. Complications included marked muscular spasticity and mental retardation and blindness. These were seen in only three patients. Toxic effects were encountered in 10 patients.

AIGNER, Rochester, Minn.

THROMBOSIS OF INTERNAL CAROTID ARTERY TREATED BY ARTERIAL SURGERY. CHARLES ROB and E. B. WHEELER, Brit. M. J. 2:264 (Aug. 3) 1957.

Twenty-seven patients with symptomatic occlusions of the internal carotid artery were treated primarily by direct surgical procedures on the artery in an attempt to restore normal blood flow. The ability to restore blood flow depended largely on whether the occlusion was partial or complete. If occlusion is complete, blood flow could be restored only during the brief period before the clot extended into the cranial cavity, and even then irreversible cortical damage occurred in three cases. Good blood flow was almost always reestablished in cases of partial occlusion. Only 2 of the 27 patients had any postoperative exacerbation of neurologic symptoms.

The authors believe that the patients most likely to benefit from surgical treatment are those with incomplete occlusions who consult a physician because of symptoms of cerebrovascular insufficiency. Restoration of blood flow not only often relieves the symptoms of cerebrovascular insufficiency but may prevent later development of complete thrombosis and irreversible cerebral damage.

ECHOLS, New Orleans.

TREATMENT OF TUBERCULOUS MENINGITIS: A COMPARATIVE TRIAL, by a Scottish Join Committee, Lancet 2:756 (Oct. 19) 1957.

The Scottish Joint Committee in England for the evaluation of treatment in tuberculous meningitis reports their conclusions based on 111 cases of tuberculous meningitis. They conclude that the results of their trial of treatment that they planned indicate that, when isoniazid is included in the chemotherapy, intrathecal streptomycin is not an essential part of the treatment schedule. In the standard group, chemotherapy was with streptomycin (by both the intramuscular and the intrathecal route) and para-aminosalicylic acid. They discovered that the return of the cerebrospinal fluid to normal was slightly more rapid in the patients receiving minimal intrathecal therapy.

YASKIN, Camden, N. J.

News and Comment

SOCIETY NEWS

The American Neurological Association.—At the 83d Annual Meeting of the American Neurological Association, held in Atlantic City, June 16-18, 1958, the following officers were elected for the coming year:

President	Bernard J. Alpers, Philadelphia
President-elect	Derek Denny-Brown, Boston
First vice-president	Paul I. Yakovlev, Boston
Second vice-president	Margaret A. Kennard, Fort Steilacoom, Wash.
Secretary-treasurer	Charles Rupp, Philadelphia
Assistant secretary	William F. Caveness, New York
Editor of *Transactions*	Charles Rupp, Philadelphia

The 84th Annual Meeting of the Association will be held at the Claridge Hotel, Atlantic City, June 15-17, 1959.

Books

BOOK REVIEWS

Ciba Foundation: Hormones in Blood (Colloquia on Endocrinology, Vol. 11). G. E. W. Wolstenholme and E. C. P. Miller, Editors. Price, $9.00. Pp. 416. J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, 1957.

Improvement in methodology for the assay of endocrine secretions as found in blood rather than urine is of vital importance to all investigators in the medical sciences. In this volume, as is true with most books, methods described therein may be obsolete, or at least modified, by the time of publication; however, basic methods are discussed by eminent workers in hormone assay procedures, making this volume of value for some time to come. In addition to very elaborate discussions on the actual assay techniques, considerable space is devoted to the questions of transport of hormones in blood and eventual inactivation of these secretions. Chemical analyses employing newly developed isotope techniques, as well as new bioassay methods, are well reviewed. Each paper is followed by a discussion contributed to by an international group of experts, permitting the reader better to evaluate the data presented. The pituitary, thyroid, and pancreas receive considerable attention, but most is given to the adrenocortical steroids, justifiably highlighting the dramatic advancements in this particular field. Thyroid hormones are splendidly discussed by the contributors to this section. This volume is highly recommended and is well worth the attention of the neurologist. Of special interest to those in neuroendocrine investigation are the sections on general principles in bioassay, factors influencing corticotropin level, and catechol hormones in blood. The existing work in competitive inhibition of the thyroid-stimulating hormone (TSH) by the acetylated TSH is reviewed by the original workers.

MELVIN HORWITH, M.D.

Ciba Foundation Symposium on Bone Structure and Metabolism. G. E. W. Wolstenholme and C. M. O'Connor, Editors. Price, $8.00. Pp. 299, with 121 illustrations. J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, 1957.

This volume on bone structure and metabolism fulfills the wishes of clinicians and investigators interested in skeletal tissue by distilling the thoughts of a group of eminent workers in this field. The list of participants, international in scope, is impressive and should at once insure lively and informative discussions. The symposium is arranged in a logical order, namely, a fundamental approach to structure and metabolism of bone, then the biochemistry and physiology. Clinical bone disorders occupy about one-half the volume. The clinician should not look for classical discussions of disorders of bone in this volume. There are, however, very refreshing attempts at answering some of the perplexing questions that remain unresolved in consideration of metabolic bone disease states and at reassessing older concepts now studied by new techniques. There are twenty formal presentations, followed by verbatim discussions by the other members of the symposium. The illustrations are excellent, though few in number. Considering the multitude of subjects mentioned in the various discussions, the subject index is quite satisfactory. This book will be welcomed by the clinician and investigator of diseases of the skeletal system, but will be of limited interest to neurologists in general.

MELVIN HORWITH, M.D.

A Frontal Section Anatomy of the Head and Neck. By Otto Frederic Kampmeier, Arthur R. Cooper, and Thomas S. Jones. Price, $15.00. Pp. 30. University of Illinois Press, 358 Administration Building, Urbana, Ill.

This atlas contains twenty full-scale photographs of coronal sections of the head and neck. All of them are of remarkable clarity, preserving the detail of a fresh anatomical section. The sections are taken approximately 1 cm. apart, making it exceptionally easy to trace the course of small structures. All of the structures are clearly labeled, and the number of labels is not so excessive as to confuse the reader. This book is handsomely bound and printed. In addition, there is a series of five drawings indicating the relationship of the

sections to the cranial bones, to the ventricular system, to a midline section of the brain, brain stem, and cerebellum, and to the intra- and extracranial cerebral venous and arterial systems. Each photograph is accompanied by a small drawing to remind the reader of the exact position of the section illustrated.

The clarity of the photography and of the labeling should make this work a valuable source of anatomical information for anyone dealing with the head and neck, and particularly for neurologists and neurosurgeons.

FLETCHER MCDOWELL, M.D.

Die Schädigung des Hirnstammes bei den raumfordernden Prozessen des Gehirns. By Dr. Hans Werner Pia. Springer-Verlag, Mölkerbastei 5, Wien I, 1957.

The authors review their series of over 2000 brain tumors from the standpoint of studying effects of increased intracranial pressure on the brain stem and ways of improving the prognosis of this condition.

Space-consuming lesions with displacement of intracranial contents result in cisternal encroachment either of brain (cisternal herniation) or of pathological tissue (cisternal tamponade). The result is specific alteration in the brain stem, depending upon the type of encroachment (herniation or tamponade), as well as the cistern involved. The acuteness of the process is an additional critical consideration stressed.

Special emphasis is accorded vascular lesions (e. g., calcarine infarction) accompanying cisternal encroachment, and the authors introduce the concept of internal occipital vein compression against the tentorial margin, with resultant distal venous hypertension, congestion and diapedesis, and secondary arterial bleeding, producing red infarctions of the occipital lobe. Of particular interest is the discussion of the role of cardiorespiratory disorders, such as emphysema in the aggravation of intracranial venous hypertension.

The clinicopathological findings noted in rostral and caudal brain stem involvement are correlated, and the significance of oculomotor disturbances (especially pupillary), hyperthermia, altered consciousness, tachypnea and tachycardia, and ultimate decerebrate rigidity in differentiating midbrain and bulbar involvement is stressed. Supplemental use of angiography in "silent" cases is essential in preoperative determination of the extent, size, and location of the lesion and of the degree of displacement and deformation of the midbrain.

Ultimate surgical therapy is inevitable and involves amputation of displaced convolutions or sectioning of the tentorial margin so as to free the brain stem, permitting subsequent attack upon the tumor, with significant reduction in the fatality rate. Preliminary cervical sympathetic block has been found invaluable in the reduction of peripheral resistance and venous hypertension. Similar conclusions were reached with respect to tracheotomy in the prevention of respiratory difficulties contributing to increased intracranial pressure.

This book represents an important contribution to the understanding of the causation of "central death" in intracranial space-consuming lesions.

Depersonalization

BRIAN BIRD, M.D., Cleveland

Introduction

The "Diagnostic and Statistical Manual" of the American Psychiatric Association,[2] which in a sense is an official catalogue of definitions, classifies depersonalization as one of the various symptomatic expressions of personality disorganization found in the category called Dissociative Reaction. In this category, along with depersonalization, are such disorders as amnesia, fugue states, and somnambulism. The "Manual" goes on to say that, although these disorders are often serious and may sometimes even appear to be psychotic, they are all neurotic and must be differentiated particularly from schizophrenia.

Textbooks on psychiatry contain only meager mention of depersonalization. Bleuler's text,[1] for example, refers to depersonalization only twice, and then in but a sentence or two. Kraepelin[4] describes the disorder very briefly as a common finding in mild depressions. Of the modern texts, Noyes'[5] gives perhaps the best account of it.

Journal articles on depersonalization are not very numerous. Nunberg,[6] in 1922, wrote one of the earliest and best articles; Oberndorf[7-12] published the most, six, and Freud wrote on the subject only once, in 1936.[3] Most authors agree that depersonalization is a common neurotic symptom which occurs mildly even in normal people and in varying degrees of severity up to a state verging on a psychosis.

Submitted for publication March 28, 1958.

Western Reserve University School of Medicine.

Clinical Description

The word "depersonalization" is simply one of several words used to describe neurotic feelings of unreality. These feelings of unreality, in turn, consist of peculiar mental sensations, which cause a kind of mental unsteadiness or unsureness. The feeling is very much like a mental faintness and is akin to confusion, head swimming, intoxication, and delirium. Feelings of unreality, which are always unpleasant and strange, bring about a dimming or blurring both of the person's sense of identity and of his sense of reality. As the main result, there is difficulty in distinguishing between personal impressions and objective observations.

Depersonalization may implicate all senses, or only one or two. In the latter case a person may experience as unreal everything he hears, yet be able to trust what he sees and touches.

Similarly, the experiencing of unreality may implicate all ego functions or may occur most strongly in relation to certain specific ones. There are three main ways in which the ego's reality testing may be affected: (1) in its conception of itself, (2) in its conception of the outside world, and (3) in its conception of time. Usually there is a mixture of the three.

1. In the first case, where the ego has an unreal conception of itself, the result is

depersonalization proper.* Here the patient's uncertainty concerns his own personality and his own identity. Most commonly this will result in doubt about various sense organs, and he will be unsure, for example, whether his eyes or ears are working accurately or whether it is all his imagination. In addition, he may have a feeling that his mind and body are numb or dead or insensitive, or that his thoughts are working too slowly or too fast.

Other feelings of personal unreality may be predominantly physical, with the result that the patient is uncertain of the position of his body, or he may have a strange feeling that his body is large or small, that it is tilted, that a film exists between his teeth or over his eyes. He may have great uncertainty in regard to touch, so that he is unable to determine what he feels, which finger is on top of which, whether he feels the seat of his chair or his own seat, etc. Or the disorder may involve body function—inability to sense with certainty that air is going in and out in breathing, or whether food is in the mouth. Or it may relate to feces and urine—uncertainty as to whether there is a need to defecate or to void.

2. The second form of depersonalization concerns a sense of unreality about the external world and is less a matter of apparent changes within the personality itself. This form is often called derealization. In it, familiar objects seem changed: Stationary ones seem to move, moving ones seem to be still, far objects seem near, close ones far away or tilted or skewed in some way; odors seem different, sounds seem shriller, food tastes odd. Whatever the area involved, the emphasis is upon uncertainty about the world rather than about the self. In many of these cases there is a resemblance to illusions, and sometimes to hallucinations.

3. The third form of unreality has to do with changes in the ego's sense of time and is called déjà vu. In this disorder, there is an unreal feeling that something now being observed has all been seen or experienced before. Déjà vu has many variants, and one form or another may appear as a solitary experience or may occur along with depersonalization and derealization.

Comment.—The essential aspect of every form of depersonalization is a distortion of the ego's powers of reality testing, a change which, above all, causes uncertainty about what is real and what is not real, what is internal and what is not internal.

Differential Diagnosis

Differential diagnosis of depersonalization is commonly a vexing clinical problem. Disorders in reality sense are so varied, and sometimes so extreme, that they can be confused with a great many psychotic, neurotic, and neurologic diseases. It is particularly important to make a distinction between depersonalization and schizophrenia. Certain depressive symptoms may also be confused with depersonalization. In the case of neurotic symptoms, there may be difficulty in separating depersonalization from obsessional doubting, from hypochondriacal bodily preoccupation, and from various conversion reactions. Finally, depersonalization must be clearly distinguished from actual anatomical disturbances in sensory function.

Some of the differential points to be considered in each of the areas can be given briefly.

1. *Schizophrenia.*—Two circumstances make schizophrenia and depersonalization a problem in differentiation. The first is that depersonalization and schizophrenia may coexist in one patient. The second is that many schizophrenic symptoms concern feelings, identity, and reality in a way that sounds much the same as the depersonalized patient's description of his feelings. This is particularly true of the depersonalized patient who has feelings of being split in

* Strictly speaking, this is the only form that should be called by this name, but in practice the word "depersonalization" is commonly used for all forms of unreality feelings.

two or of having two personalities or two parts, or who says he has no feelings or has dead feelings. All these symptoms sound like the somatic delusions of schizophrenics. But there is a fundamental difference. To the psychotic patient, a delusion is a fact and is treated in concrete, absolute fashion as if it were an object. For example, "My mind *is* split or twisted or dead; my eyes *do not* see; my ears *do not* hear; I *have* no stomach, no feelings," etc. By contrast, the unreal feelings of a depersonalized patient are all qualified by a real feeling; for example, "I *feel as if* my thoughts are dead, *as if* I were two people, *as if* my eyes don't see," etc.

The visceral hallucinations of schizophrenia may be even harder to distinguish from neurotic feelings of unreality. But, again, as with delusions, the hallucination is complete in itself; it is a self-satisfying, concrete fact. For example, "Something *is* loose in my head; I *hear* it dripping behind my eyes"; or, "Everything I see *is* left-sided"; or, "My ears *are* tuned up so everything is twice as loud." The depersonalized patient may describe his experiences in much the same way, but his description will be prefaced by "I feel as if." Furthermore, when closely questioned, he will recognize and admit that he actually sees and hears well—it is just that everything *seems* different.

2. *Depressive Reactions.*—In addition to the difficulty presented by the simultaneous occurrence of depersonalization and depression, there is the problem of differentiating depressive delusions from depersonalization. The melancholic patient, particularly, may say that his feelings are dead, his head wooden, and that his mind and his body have stopped functioning. These are true delusions and are not to be regarded as feelings of unreality.

3. *Obsessive-Compulsive Psychosis.*—Obsessional doubting is another disorder that is often very difficult to differentiate from depersonalization. The doubter does not know whether he heard something or read it; he is not sure precisely when he did something or whether he did it all, or perhaps he is in doubt as to exactly who it was he met, etc. The doubter sounds very much like the patient with feelings of unreality who is uncertain about many real events. However, the obsessional doubting occurs more in the area of internal thoughts, whereas depersonalization typically involves external matters perceived by the various sense organs.

4. *Hypochondria.*—Depersonalization may resemble hypochondria, especially when feelings of unreality center around taste, smell, and body sensations. In such cases the depersonalized patient will seem to be preoccupied with bodily symptoms. Actually, however, he is preoccupied with the question of whether what he senses is real, and not with disease as such. He is concerned, for example, about whether his hunger feelings are real or imaginary, whether food is appetizing or not, whether his breath is shallow or deep—and not about nutrition or about getting enough air into his lungs.

5. *Conversion Symptoms.*—Conversion symptoms sometimes merge into depersonalization in a way that makes differentiation impossible. This is true especially of symptoms like faintness, head swimming, limb weakness, and paresthesias, all of which have some quality of unreality. However, it is still often possible to discriminate between the two. The conversion symptom stresses a change in function. Depersonalization stresses the reality or unreality of function. For example, depersonalization is not expressed as a feeling of weakness in vision but as uncertainty as to whether what is seen is real or not.

6. *Biological Disease in Sensory Systems.*—The problem of differentiating depersonalization symptoms from other neurotic symptoms is not always of great importance. However, it is important to differentiate depersonalization from symptoms arising out of actual anatomical disturbances in sensory systems.

Differentiation can usually be made, first, by neurologic examination and examination of the sense organs, and, second, by study of the nature of the symptom. In depersonalization there is no loss of perception. Events are seen and heard accurately. It is only after they are recorded that the distortion takes place; i. e., it is an ego-initiated distortion.

Etiology

Depersonalization is found in so many pathological conditions that it would be useless to enumerate them. As a generalization, however, it may be said that depersonalization can be caused by any disorder that seriously weakens the ego. Depersonalization is, accordingly, a frequent finding in psychosis, high fever, organic brain disease, toxic states of any kind, and in cases of severe physical and mental stress.

The Mechanism and Meaning of Depersonalization

Depersonalization, although it seems utterly useless and, in fact, is often extremely objectionable, does have many purposes that are easily recognized. To illustrate some of these purposes, as well as to trace to some extent the general mechanics of depersonalization, I shall describe a clinical case.

A 15-year-old boy, in analysis for over a year, suddenly developed an acute state of depersonalization. The attack began at school with a frightening feeling that he could no longer understand what he saw or heard. "I'd know what I heard and what I saw," he said, "but it didn't register. Nothing made sense. I couldn't understand a single thing—just as if I weren't I. I was in a panic. I thought I was really crazy. I was like two people, split in two. I was neutral. I had no feelings for anyone, and nothing got through to me. It was as if I was insulated from everything."

Another reaction was the patient's fear of asking questions in class—he was afraid he was in the wrong class, or that no class was there, or that he had already asked the question, or that the wrong words might come out. Similar difficulties occurred at home and at play.

The patient's acute depersonalization lasted only a few weeks. Then, when its components were analyzed and the underlying conflicts were to some extent worked through, the symptom disappeared.

Analysis of the symptom proceeded something like this. The patient's unreality was interpreted as a defense, and he was told that there must be some observation or event which he wanted to disbelieve, and that if he made everything unreal, the frightening observation or event would become unreal, too.

The patient readily admitted that there was something of which he was desperately afraid. His fear centered around a recently acquired girl friend. Because he had a strong fear of girls and until now had never really had a girl friend, not only was he afraid that this one would reject him, he was also afraid she would not. His fears were accentuated by jealousy, a feeling formerly foreign to him. Also new and foreign at this time were feelings of anger. This boy normally got angry only rarely, but now in his jealous state he thought he might become angry if another boy tried to take his girl away.

Then a boy did just that, and the girl, who until now had returned the patient's affection, went out with this other boy. The patient became intensely jealous and was afraid of what would happen when he saw the girl again. What he feared, first, was that she would reject him, would tell him that she wanted nothing more to do with him. Second, he feared just the opposite, that she would say she loved him and would offer herself to him. Depersonalization, which began while he was on his way to school and a meeting with his girl, was evidently the patient's way of preparing himself for either of these two shocks. If everything he heard was unreal, anything he might hear from her would also be unreal.

So far, so good. But, unfortunately, symptoms do not always clear up when their immediate cause is discovered. This patient's depersonalization not only continued; it got worse. What I did then was simply to continue the interpretation that the patient was warding off shocking observations.

Through further associations, the patient led the way to a discovery of a number of these events. He began by recalling a series of shocking accidents that had happened to him in the past. Then he went on to tell about his first ejaculation when he was 13, and how shocking that was. It happened one night when he had been masturbating in the dark. All of a sudden he had an orgasm. The orgasm itself was shocking enough, but, in addition, he thought the semen, when it came, was blood. He was so frightened that he could not bring himself to look at his penis, and he spent the entire night in a state of painful uncertainty. These feelings of unreality, although unpleasant, served the purpose of warding off a worse pos-

sibility, viz., that he had really injured his penis and was bleeding to death.

This was an interesting and significant discovery. But even it did not cure the patient's depersonalization. However, there was a change, in that he now reported that the feelings of unreality came on most acutely when he was in the presence of girls, particularly when girls exposed too much of their bodies in shorts or bathing suits. It was then that his sense of reality faded and everything became uncertain.

This reaction to exposure I interpreted as meaning that, as a child, he must have experienced a strong shock at seeing little girls naked and discovering their lack of a penis, that he then must have concluded that the same thing could happen to him, and that, to ward off this fear, he made what he saw unreal.

This interpretation was supported by subsequent associations. The patient recalled several disturbing incidents, from the age of 5, of being caught inspecting a girl's genitals and being punished for it. Significantly, in spite of punishment, he continued to examine girls' genitals. He felt there was something he must see, but he did not know what it was. And when he looked, he was never satisfied—he had to look again. This repeated looking apparently stemmed not only from his disbelief of what he saw each time but also from the hope that something would turn up as if by magic.

Still, even when we learned these things, the patient's symptom continued.

But now another aspect of it took the spotlight. In connection with his depersonalization he had many ideas of reference—of being overheard, or of overhearing others in secret conversation. These associations and others led me to interpret his sense of unreality as representing, among other defenses, a defense against hearing sounds coming from his parents' bedroom, sounds of sexual intercourse. As a child, I told him, he must have heard such sounds and was so overcome he had to deny them by making them unreal.

Following this interpretation, there was a period of several days or a week in which primal-scene material was predominant. The patient himself began by saying that he must have *seen* his parents in intercourse, in addition to hearing them, because now in his symptom the things he saw as well as the things he heard were unreal. He then remembered that one morning several years earlier he had actually burst uninvited into his parents' bedroom and had been told by them to get out, very much as now he was afraid his girl would tell him to get out.

Then, quite unexpectedly one day—for the patient rarely got even slightly angry—he came to his treatment hour in a state of great anger. He was furious with his girl. At school that afternoon one of his classmates had told him his girl was alone in a certain room with another boy. The patient went to this room, burst in, and found the two alone there. He left immediately, feeling hurt and rejected. These feelings were replaced by ones of anger, and now anger ruled everything.

The similarity between his bursting in upon his girl and bursting into his parent's bedroom was so striking that I simply drew his attention to it and said he must have been very angry with his parents. As soon as I said this, the patient recalled that that very morning the same thing had happened: on some pretext or other he had burst into his parents' bedroom and had been told abruptly to get out. He had not felt angry or hurt at the time, but now, while thinking about it, he did feel very angry.

Discovery of this material, centering around his anger and the primal scene, brought a quick end to the patient's depersonalization. He experienced no more feelings of unreality. It was as if, having finally permitted himself to recognize the main observation he was warding off, viz., parental intercourse and the loss of his mother, and having finally permitted himself to react to his suffering with a normal expression of anger, there was no longer any need for the defense of depersonalization, and it therefore evaporated. Not only did the symptom clear up but the patient became much more realistic in many other ways as well.

Analysis of the Clinical Material

Thorough study of this patient's case, and of supplemental material from other patients and from other reports on depersonalization, gives rise to many formulations, both clinical and theoretical. Some of the main ones can be presented briefly.

1. *Depersonalization as a Defense.*—In considering any neurotic symptom, I like to start with the question: What good is it; what is it doing for the patient? Too often we think of symptoms as artifacts, or as nuisances to be gotten rid of. Too often we forget that a symptom is always created by the ego to serve a definite purpose. In that sense a symptom always has a positive aim: It is working *for* the patient. This is the aspect of a symptom I look for first.

In this patient the most striking use of depersonalization was as a defense. Simply by making everything he perceived unreal, he was able to ward off accepting the reality of specifically painful observations. Among

the observations that he repudiated in this way were the fear of rejection or acceptance by his girl, the fear that he had injured his penis by masturbation and ejaculation, the fear of castration provoked by seeing girls' genitals, and, finally and most significantly, his excitement, fear, and anger at observing his parents in intercourse.

Clinically, I think it is very helpful to keep this defensive meaning of depersonalization uppermost in mind. In any patient with feelings of unreality, one can profitably wonder what frightening occurrence the patient is trying to ward off. This defense is particularly common in depersonalization accompanying physical disorders. Very often the feelings of unreality of the organically ill patient are caused by, or at least used by, his wish to avoid facing the reality of his new physical disorder. In many of these organic patients, depersonalization can be cleared up simply by helping the patient to face and to understand the full import of his body disease. Very often the truth, although painful, is much more acceptable than vague suspicions; and once the truth is fully understood, there is no need to make it unreal.

2. *Depersonalization Is a Hysterical Symptom.*—The second point I should like to make is that depersonalization is not merely a defense; it is as well a true hysterical symptom. In fact, it is very much like a conversion symptom and is produced in the same way as, for example, hysterical paralysis of a limb. Normally, the function of the conscious part of the mind is to remain calm in its task of objectively recording internal and external stimuli, no matter how disturbing these perceptions may be. In depersonalization this function of consciousness breaks down. Instead of simply recording perceptions, consciousness becomes affected by them; it becomes libidinized or sexualized and then reacts as if it were a sexual part of the body. Once this happens, the ego is forced to inhibit or to distort various conscious functions in such a way as to disguise their now sexual nature. This procedure is identical with the manner in which the function of a limb, if it becomes libidinized, is inhibited by the ego and becomes paralyzed.

The general hysterical nature of depersonalization is important to remember because, knowing this, one can rely on the disorder to follow the same course, to react to the same stimuli, and to use the same mechanisms as other forms of conversion. Thus, in all cases of unreality, one should look for the presence of erotic stimuli so disturbing that they are sexualizing consciousness. With my patient it became clear, after awhile, that his unreal feelings occurred only when he was in the presence of people who had a sexual meaning to him, or when he had erotic thoughts, or when he was stimulated by girls in swim suits.

3. *Nature of the Loss of Reality in Depersonalization.*—A third point about depersonalization is that the loss of reality involved is distinctly different from the loss that occurs in psychosis. In psychosis the break with reality protects the patient from reality. In depersonalization the feelings of unreality protect the patient from breaking with reality. It works in this way: When certain observations or feelings come up which threaten a person's relation with someone important to him, a number of courses are open to him: He can continue the relationship as it is and take a chance on its being destroyed, or he can voluntarily reduce the intensity of the relationship to a point where it is no longer threatening, or he can produce neurotic symptoms which allow him to remain in touch with his desired object, but in a restricted or distorted way. One of the most effective of these protective symptoms is depersonalization. In a state of depersonalization, the patient can permit himself to make all sorts of painful observations and to have all kinds of disturbing feelings because, by making them seem unreal, he neutralizes them. It is like put-

ting insulation between two objects so that they may stay close together.

My patient showed this aspect of depersonalization in many ways. He even stated it in his own words: "I feel cut off from everybody. I make no impression on them, or they on me." This insulating characteristic allowed him to continue actual contact with his girl. Without the symptom, he might have had to avoid her altogether.

His unreal feelings also allowed him to continue to see me. He had many disturbing feelings when with me, but, because they were unreal to him, they could be tolerated and my presence could be tolerated. Strikingly, his feelings of unreality often came on as he entered my office, and left as he left. This is not an uncommon finding, and, in general, whenever a patient says that his unreal feelings, or his faintness, or his dizziness, comes on when he sees his doctor and leaves when he leaves the doctor, one may be sure that these sensations are in some degree a protection which makes it possible for him to see the doctor at all. Accordingly, one should not be too unfriendly to a patient's depersonalization. Sometimes it is his only means of clinging to reality.

4. *Origin of Depersonalization.*—Perhaps the most important aspect of depersonalization is its origin, its place in the patient's developmental history. Theoretically, since it is a state in which there is uncertainty as to what is object and what is self, depersonalization may be regarded as a return to the time in earliest infancy when there is no differentiation between objects and self.

At birth, and for some weeks after birth, the infant, as far as anyone knows, is not yet aware that objects exist. The infant merely experiences sensations, without being at all concerned where they come from. Accordingly, he still has no sense of reality. Reality sense develops only as the ego develops and as the reality principle takes over from the pleasure principle. The ego begins this recognition of reality, however, not by identifying objects as such but, very simply, by identifying the borderline between its own body and other objects. Once this line of division is recognized, the infant then has a chance to determine which is on which side of the line, self or objects. Of primary importance as the infant's first objects are the mother and the parts of her body, especially her breasts, her hands, and her face.

The development of an awareness of reality constitutes the birth of the ego and is very much like actual birth. In both cases —whether body or ego—the infant separates off from the mother. This separation in either case, however, is not sudden or complete. Even bodily birth, although it seems like a complete separation, is not complete. The infant remains entirely dependent upon the mother and attached to her body (through her breasts and her hands) for a long time to come. Likewise, for many months, and even years, the infant's ego is closely attached to and is a part of the mother's ego. She thinks, feels, and acts for him, and, conversely, everything he does affects her.

Although birth of the ego is a progressive movement toward an increasing awareness and definition of reality, it is not consistently progressive, nor is it always, or perhaps ever, complete. No one perhaps ever completely breaks away from his mother and establishes himself as a solitary figure surrounded by alien objective reality. Always there is a tie to, and a pull back to, the original complete union with the mother. Depersonalization is one manifestation of this attempt to relive the original, undifferentiated state, in which no reality exists.

Actually, however, depersonalization, like all neurotic symptoms, is a compromise: It represents not only a wish to return ultimately to the mother's womb but an attempt to ward off such temptation.

In my patient's case, this aspect of depersonalization was very clear. One of his major problems was a pathologically intense attachment to his mother. He could

not tolerate thinking about the time when he would have to leave home, and even temporary separations threw him into attacks of anxiety. But he was just as afraid to get too close to his mother. His wish to be completely united with her was a very frightening thing. It was frightening because, if achieved, it would mean losing his own identity, especially his own masculine identity.

With his girl friend, my patient showed the same two fears. He feared not only that she would reject him, but just as much that she would give herself to him and he would be lost in union with her. Significantly, just before his attack of depersonalization, and while he was developing his relationship to his girl friend, he had many pleasant daydreams of being sealed in a cave or in a sleeping bag or in water. In every case the situation was one which would be dark and warm and free from all stimuli. His associations to these daydreams were of being a baby in his mother's womb.

Freud, in one of his few mentions of unreality, comments on this relation to the mother. In the "Interpretation of Dreams," he says that in déjà vu dreams, the feeling that "I have seen this before" or "I have been here before" can relate only to one place: the mother's genitals.

Clinically, an understanding of this infantile meaning of depersonalization is often very helpful. Whenever a patient reports any symptom dealing with unreal feelings, he is very likely close to material having to do with the mother, and particularly with primal-scene ideas, memories, and conflicts.

5. *Unreality and Anger.*—A further aspect of depersonalization also relates to the earliest days of reality-sense development in infancy. The act of being born—whether it be the body or the ego—is never an experience free from pain. Facing reality and breaking away from the mother are always painful and come about only under pressure.

Accordingly, from a knowledge of this early connection between pain and reality, one can theorize that pathological states of unreality may also relate to pain and suffering and to its reaction, anger. More specifically, depersonalization and other states of unreality may be instituted by the ego in order to ward off not only pain but also anger.

This relationship was certainly true in the case of my patient. For years he had been unable to allow himself to have any feelings of anger, and for years he had been most unrealistic. One emotional state supported the other. By making painful observations unreal, there was nothing to be angry at. By inhibiting anger, everything lost some of its reality. This was most clearly demonstrated in relation to his witnessing his parents in what he later assumed was intercourse. Because he paid no attention to what he saw, there was nothing to be angry at. When, however, he permitted himself to recognize his hurt and his anger at the primal scene represented by his girl and another boy, there was no room for unreality—or no need for it.

Clinically, the relationship of anger to reality is a very useful observation. When patients show an extreme lack of anger, one should be suspicious that they are also very unrealistic. Conversely, when patients are neurotically confused and have feelings of unreality, one should immediately suspect that they are angry about something.

This confusion-anger response is seen commonly in medical and surgical patients. Many surgical patients who, after surgery, are almost idiotic in their unrealistic confusion, prove, upon study, to be angry with their surgeon, or the nurses, or even cruel fate, which has dealt them this unfair surgical blow. In such cases, if the anger can be found, the confusion disappears.

A person cannot be truly angry and unrealistic at the same time!

6. *Reality and Bodily Knowledge.*—Because accurate observations of reality de-

pend so largely on distinguishing what is object and what is personal, it follows that any degree of unreality will be accompanied by ignorance about the self. This ignorance will involve knowledge not only of the ego but of the body as well. And, of course, the opposite will be true, too—if for any reason a person avoids familiarity with his own body, he will likely be found to have corresponding blind spots about what goes on around him.

These are very real, earthy phenomena and are observable over and over in clinical practice. A surprising number of persons are actually very poorly informed about their own bodies, particularly about any bodily part which has a sexual or narcissistic meaning to them. Perhaps they have never really looked at their genitals, anus, or breasts; perhaps they have never really studied their facial contours, muscular development, or waistline. I once had a patient in analysis who weighed 325 lb. One day I asked her if something or other had to do with her being fat. She was stunned. No one before had ever said she was fat, and she never thought of herself as being fat. Overweight, yes. Somewhat obese, yes. But fat, never! Other examples are people who have hearing or sight defects, yet are not really aware of the extent of the loss. In all these cases there is a corresponding defect in reality sense, and the person will have cordinate difficulties in accurately perceiving many business, professional, and personal matters.

An example follows: A scientist in analysis with me had great difficulty in his work deciding what was a good result and what was not, whether to pursue one line of investigation or another. He reworked his data endlessly, and repeatedly overlooked both obvious errors and just as obvious confirming findings. One day, after working on this problem for months, he made a casual observation about his penis—that it was too big. Without much thought, I said, "What do you mean—too big?" At once he was thrown into a state of confusion, similar to the confusion about his work. He found he knew very little about his penis, being unsure even whether he was circumcised. A few days later he reported that he had for the first time in his memory really looked at his penis. He was shocked at what he discovered: It was not so big; it was mottled and discolored, had prominent veins on it, etc. But in spite of being shocked, he was very relieved—now he felt he really knew something about himself. But even more rewarding was the effect upon his work. At once he began to see his research more clearly. He found many hidden data and was able to work freely toward the conclusion of many lingering problems.

The relationship of a person's feelings about his body to his picturing of reality is dramatically demonstrated in patients whose bodily outline has been changed by surgery. Amputations particularly tend to have a disturbing effect upon one's view of the world.

The importance of bodily knowledge to an understanding of reality is also well expressed by the common saying, "I had to pinch myself to be sure it was true."

7. *Unreality as a Character Trait.*—Inability to see things realistically occurs not only as an acute hysterical symptom but also as an ego-syntonic, permanent part of the personality. Actually, this may be the worst form, more injurious in many ways than depersonalization. Depersonalization, because it is ego-alien, is at least recognized by the ego as abnormal and is fought against and gotten rid of as soon as possible. Characterological unreality, on the other hand, is so smoothly integrated into the personality that it is not alien, not irritating, and not even recognized as existing. Accordingly, the ego does nothing to change the situation. All that happens is that the person increasingly views things in such a way as to avoid anger and pain, and perhaps other feelings as well.

On the other hand, a certain amount of unreality in a person's make-up is essen-

tial: It allows him to go ahead and do many things which otherwise he would not be brave enough to do. But beyond a certain point the benefit is lost and the situation reaches handicap proportions. As a safeguard against an encroaching lack of realism, it is very helpful to take a second look at the world once in awhile just to be sure that the way we see things is, after all, the only possible way for them to be seen.

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Effects of Lysergic Acid Diethylamide (LSD-25) on Intellectual Functions

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I. Memory

Introduction.—The results of previous studies of the effect of lysergic acid diethylamide (LSD-25) on memory suggest that the minimal dose level at which impairment becomes evident lies somewhere between 50μg. and 100μg. Sloane and Lovett Doust,[1] working at the 40μg. level, and Jarvik et al.,[2] working at the 50μg. level, found little or no evidence of memory impairment in their studies. However, the latter investigators reported that when the dose level was raised to 100μg., scores were significantly lower on four of the five visual tests and on two of the four auditory tests that they employed. Bercel et al.,[3] who used 1μg/kg. body weight, also found evidence of impairment, but they studied memory for only one kind of material, a series of unrelated test words. The purpose of the present study was to determine whether memory for various kinds of material is differentially affected by LSD-25 at a dose level between 50μg. and 100μg.

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The Psychiatric Institute, University of Maryland.

The studies reported in this paper were conducted under the guidance and supervision of Dr. Jacob E. Finesinger, Director of the Psychiatric Institute.

Procedure.—The subjects were 16 male college graduates between the ages of 20 and 24, each of whom had had a physical examination and a psychiatric screening interview prior to the start of the study. The Wechsler Memory Scale[4] was administered to the subjects under control conditions, and also after they had ingested 72μg. of LSD-25 in distilled water. Half the sample was tested first under control conditions, and again two days later between one and one-half and three and one-half hours after ingesting the drug. For the other half, the order of the two conditions was reversed. Similarly, the administration of Form I of the Memory Scale preceded the administration of Form II for half the sample, while this order was reversed for the other half.

Results.—A preliminary analysis of the data gave no evidence of significant practice effects or of systematic differences in the two forms of the Memory Scale, and so the data for all subjects were pooled. Median scores under control and drug conditions are shown in Table 1. To evaluate the significance of the results, Wilcoxon's matched-pairs signed-ranks test[5] was employed. Scores on six of the seven subtests were lower in the drug state than under

TABLE 1.—*Median Scores on the Wechsler Memory Scale Under Control and Drug Conditions*
N=16

Subtest	Control	Drug	P*
Personal and Current Information (How old are you? Who is President of the United States? etc.)	5.9	6.0	
Orientation (What year is this? What is the name of the place you are in? etc.)	5.0	4.9	
Mental Control (counting backward, saying the alphabet, performing serial addition)	8.8	7.8	0.05
Logical Memory (reproduction of brief prose passages)	13.5	10.2	0.01
Memory Span (repetition of series of digits, forward and backward)	12.0	11.0	
Visual Reproduction (drawing simple geometric figures from memory)	12.5	10.8	0.01
Associate Learning (paired associates: easy, e. g., metal-iron, and hard, e. g., crush-dark)	14.8	14.5	
Memory Quotient	113.8	97.0	0.01

* Based on Wilcoxon's matched-pairs signed-ranks test.

control conditions, but only three of the differences attained the conventional levels of significance. For the Memory Quotient, which is based on the sum of scores on all the subtests, the difference was highly significant.

Comment.—The results of this study, in conjunction with those of earlier investigators, indicate the minimal dose levels of LSD-25 at which impairment of memory for various kinds of material becomes evident. In Table 2, the findings of the different studies are compared. The Table shows that the minimal dose level required to impair memory for prose passages lies between 50μg. and 72μg; for series of digits, above 100μg.; for geometric figures, between 40μg. and 72μg., and for paired associates, between 72μg. and 100μg.

Jarvik et al.[2] have observed that the results of such studies as the present one "do not indicate whether the impairment [produced by LSD-25] is due to the inability to learn, the inability to retain, or the inability to express what has been remembered." In tests of immediate memory, the interval between the learning of the material and the test of its retention is so brief that inability to retain probably cannot be distinguished from inability to learn. However, it should be possible to estimate the extent to which impairment is due to inability to express what has been remembered, by substituting tests of recognition for tests of recall or reproduction.

Finally, it should be noted that this study has dealt with only one aspect of the effect of LSD-25 on memory. No data, for example, have been presented on the subject's ability to recall at a later date the events that took place while he was under the influence of the drug. From the literature, one receives the impression that the subject's memory for his experiences in the drug state is unaffected, but we have often observed at least partial amnesia for these experiences on the day following the ingestion of the drug.

Summary.—LSD-25 in doses of 72μg. significantly impaired memory for only certain kinds of material, as measured by the Wechsler Memory Scale. On the one hand, the ability to draw geometric figures from memory, the ability to reproduce brief prose passages, and the ability to count backward, say the alphabet, and perform serial addition were all affected by the drug. On the other hand, the ability to learn paired associates, the ability to repeat series of digits, orientation for time and place, and memory for personal and current information appeared to be unaffected by the drug at the dose level employed.

TABLE 2.—*Presence or Absence of Impairment of Memory for Various Kinds of Material as a Function of Dose Level* *

Material	40μg.†	50μg.‡	72μg.§	100μg.‡
Prose passages	—	—	+	+
Series of digits	—	—	—	—
Geometric figures	—		+	
Paired associates		—	—	+

* Blank spaces indicate that memory for the material in question was not tested in the particular study. Presence of impairment is indicated by the plus sign (+); absence, by the minus sign (—).
† Sloane and Lovett Doust.[1]
‡ Jarvik et al.[2]
§ Present study.

II. Abstract Thinking

Introduction.—Previous studies of the effect of LSD-25 on abstract thinking have yielded inconclusive results. Isbell et al.,[6] working with tests from the Goldstein-Scheerer battery, and Primac et al.,[7] working with the Wisconsin Card Sorting Test, found no evidence of impairment in their studies. Levine et al.,[8] who used the Wechsler-Bellevue Intelligence Scale, concluded that LSD-25 does impair abstract thinking. Most pertinent to the present paper are the observations of DeShon et al.,[9] who studied clinically the effect of the drug on proverb interpretation: "While the responses were predominantly concrete, a wide range of abstractions was still revealed, with a significant number of answers lying in the overgeneralized tangential area of the concrete-abstract spectrum." These investigators likened the interpretations given by normal subjects under the influence of LSD-25 to those given by schizophrenics.

We have routinely used proverb interpretation in the mental-status examination of subjects under the influence of the drug, and have been impressed by the concreteness of the responses obtained. Subjects asked what is meant by "A rolling stone gathers no moss," for example, have tended to respond literally in terms of stones and moss, instead of translating these symbols into the abstractions that they represent. The publication of the Gorham Proverbs Test[10] provided an opportunity to check rigorously the clinical impression that LSD-25 does impair the ability to interpret proverbs. Recent studies have demonstrated that the Proverbs Test can differentiate both organic and schizophrenic patients from normal subjects who have been matched with the patients for intelligence.[11,12]

Procedure.—The subjects for the study of proverb interpretation were the same as those employed for the study of memory, and the same research design was used in the two studies. The Proverbs Test was self-administered between two and four hours after the subjects had ingested LSD-25, directly following the administration of the Wechsler Memory Scale.

Results.—All the test records were scored by two judges, with a reliability of 0.92 (Spearman's ρ), demonstrating the relative objectivity of the Proverbs Test. A preliminary analysis of the data gave no evidence of significant practice effects or of systematic differences in the two forms of the test (Clinical Forms I and II), and so the data for all subjects were pooled. The quantitative results were as follows: Under control conditions, the subjects obtained a median score of 19.5; after ingestion of LSD-25, the median score dropped to 13.5. The difference in scores under the two conditions was significant at the 0.01 level, as determined by Wilcoxon's test.

A qualitative analysis of failures (responses receiving no credit or only partial credit) under the two conditions was also carried out. Following Terman and Merrill,[13] two major types of failures were distinguished: concrete responses, in which the proverb was taken literally; and incorrect abstractions, in which the symbols were translated into abstractions, but inaccurately. The following examples were actual responses to the proverb "When the cat's away the mice will play": concrete response—"There's no cat to watch, and so the mice have a good time"; incorrect abstraction—"If no authority is present, a group ordinarily will revolt if given the opportunity." The subjects had failures of both types not only under the influence of the drug but also under control conditions, with incorrect abstractions predominating in both cases.

Comment.—The results of the quantitative analysis resemble those obtained by Gorham in a study of chronic schizophrenics and normal subjects, matched for intelligence. Considering only the findings for subjects of high intelligence, roughly comparable to the college graduates of the present study, Gorham's normal group obtained a mean score of 19.2, while the mean score of the schizophrenic group was 12.6. In the present study, the corresponding (control and drug) median scores were 19.5 and 13.5, respectively. The similarity in the results of the two studies suggests the desirability of a rigorous comparison of the interpretations of schizophrenics with those of normal subjects under the influence of LSD-25, employing qualitative as well as quantitative analytic techniques.

The findings of the qualitative analysis were not consistent with earlier clinical impressions, in that the majority of failures in the drug state were not concrete responses, but rather incorrect abstractions. This discrepancy may be due to the fact that in preliminary work the proverbs were presented orally and oral responses were required, whereas in the study the proverbs were presented in printed form and the responses called for were written ones. Perhaps subjects respond on a higher level of abstraction in writing than they do orally,

but there is no empirical evidence on this point.

Summary.—LSD-25 in doses of 72 μg. significantly impaired abstract thinking, as measured by the Gorham Proverbs Test. The difference in scores under control and under drug conditions resembled the difference reported in the scores of normal subjects and chronic schizophrenics. Contrary to expectations, incorrect abstractions were commoner than concrete responses not only under control conditions, but also in the drug state.

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Thiopropazate Hydrochloride (Dartal) Chemotherapy for Emotional Disorders

A Clinical Evaluation

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Thiopropazate hydrochloride (Dartal), or 2-chloro-10-{3-[4-(2-acetoxyethyl)piperazinyl]propyl}phenothiazine, dihydrochloride, is a recent addition to the ataractic group of compounds.

Method

Employing a "double-blind" procedure, with patients serving as their own controls, and with a minimum period of two weeks on drug and two weeks on placebo, we studied intensively a heterogeneous group of 84 psychiatric outpatients and 20 psychiatric inpatients. The dosage varied from 5 mg. twice a day to 30 mg. four times a day, the usual dosage being 10 mg. by mouth four times daily. All clinical evaluations were made by us, using a psychiatric rating profile which incorporated 12 categories of mental-status functioning and was graded on a 5-point scale, plus a doctor's-estimate-of-improvement rating based on a separate 4-point scale.

After control mental-status and laboratory determinations, the examinations were repeated at the end of the second and fourth weeks for the outpatients and weekly for the inpatients, and at monthly intervals thereafter. Many patients remained on the drug for several months. Laboratory studies included hemogram and urinalysis on all patients, the inpatients being followed additionally for blood urea nitrogen, fasting blood sugar, liver profile, weight, blood pressure, pulse, and temperature studies. Nine patients had bone-marrow biopsies while on the drug, and two patients had bone-marrow determinations done before and after starting the drug. No patient was on other somatic therapy during the study.

Nonparametric tests of whether two independent samples are from the same or from different populations were used to determine the validity of comparing the group starting on drug with the group starting on placebo. The hypothesis of no initial difference between the two groups was regarded as tenable for 18 of 22 characteristics recorded for the patients.

For the group starting on drug, the ratings on the doctor's-estimate-of-improvement scale and the severity of psychiatric symptoms were compared with those for the placebo group after two weeks of therapy. For the group starting on placebo, the ratings at the end of the first two weeks when the patients had been receiving placebo were compared with the ratings after the second two weeks during which the same patients had been receiving the drug. A similar analysis was not made for the group starting on drug because of the persistence of the effects of the medication.

Findings

The over-all subjective evaluation of the patients' psychiatric condition while receiving the drug revealed definite improvement for 52 patients, slight improvement for 25 patients, no change for 11 patients, and an increase in severity of symptoms for 13 patients.

At the end of the first two-week period, proportionally more improvement was shown by the 59 patients receiving thiopropazate hydrochloride than by the 45 patients receiving placebo, with a probability of less than 5 in 100 that so great a difference between the two groups occurred by chance alone. For the group starting on placebo, significantly greater improvement was shown when the patients were given the drug, and here the probability that so great a difference occurred by chance alone is less than 1 in 100. For example, after the first two-week period 54.2% of the patients starting on drug showed definite

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Tulane University School of Medicine.

Dartal was supplied by G. D. Searle & Co., P. O. Box 5110, Chicago 80.

TABLE 1.—*Effect of Thiopropazate Hydrochloride on Symptoms*

Symptom	Group	No. Observed with Symptom	Percentage of Those Originally Observed with Symptom Showing Change			
			Definite	Slight	Unchanged	Worse
Affect flattened	D	47 79.7%	8.5	27.7	61.7	2.1
	P	35 77.8	5.7	11.4	80.0	2.9
Affect inappropriate	D	26 44.1	11.5	30.8	57.7	0
	P	20 44.4	10.0	20.0	65.0	5.0
Association defect	D	26 44.1	15.4	46.2	26.9	11.5
	P	19 42.2	5.3	15.8	63.2	15.9
Depersonalization	D	47 79.7	29.8	27.7	40.4	2.1
	P	34 75.6	5.9	29.4	58.8	5.9
Mood depressed	D	31 52.5	19.4	29.0	48.4	3.2
	P	38 84.4	23.7	28.9	42.1	5.3
Anxiety	D	54 91.5	44.4	16.7	31.5	7.4
	P	38 84.4	13.2	31.6	44.7	10.5
Delusions	D	37 62.7	24.3	27.0	45.9	2.7
	P	29 64.4	6.9	20.7	62.1	10.3
Hallucinations	D	29 49.2	24.1	37.9	37.9	0
	P	17 37.8	23.5	23.5	47.0	5.9
Sociability withdrawn	D	39 66.1	17.9	17.9	61.5	2.6
	P	37 82.2	2.7	13.5	81.1	2.7
Insomnia	D	39 66.1	30.8	23.1	33.3	12.8
	P	28 62.2	17.9	17.9	53.6	10.7
Anorexia	D	26 44.1	34.6	26.9	26.9	11.5
	P	27 60.0	18.5	11.1	66.7	3.7
Amenability to psychotherapy	D	45 76.3	0	24.4	75.6	0
	P	20 44.4	0	15.0	80.0	5.0

improvement, 23.7% slight improvement, 13.6% no improvement, and 6.8% an increase in severity of disturbance, whereas of the patients starting on placebo 33.3% showed definite improvement, 15.6% slight improvement, 26.7% no improvement, and 20.0% an increase in severity of disturbance.

During the first two-week period, the group receiving thiopropazate hydrochloride showed a highly significant ($P<0.01$) reduction in the severity of the following symptoms: association defect, depersonalization, anxiety, and delusions. The drug was also effective ($0.05>P>0.01$) with symptoms of withdrawn sociability, flattened affect, and anorexia. For the group starting on placebo, significant reductions ($P<0.02$) were shown for anxiety, withdrawn sociability, and association defect after drug therapy was instituted. The only symptom for which placebo was more effective than drug was mood depression. These results are presented in detail in Table 1.

The effects of thiopropazate for the various diagnostic categories are presented in Table 2. Of 62 chronic schizophrenic patients treated, 30 (48.4%) showed definite improvement; and of 19 acute schizophren-

TABLE 2.—*Effects of Thiopropazate Hydrochloride Correlated with Diagnosis*

Diagnosis	Total	Worse	No or Only Slight Improvement	Definite Improvement
Schizophrenia, chronic				
Simple type	1	0	1	0
Catatonic type	3	0	1	2
Paranoid type	12	0	7	5
Undifferentiated type	38	9	10	19
Schizoaffective type	3	0	1	2
Childhood type	3	0	2	1
Residual type	2	0	1	1
Schizophrenia, acute				
Paranoid type	9	0	4	5
Undifferentiated type	10	1	3	6
Involutional psychotic reaction	1	0	0	1
Psychotic depressive reaction	4	0	3	1
Paranoid reaction	2	2	0	0
Psychoneurotic disorders				
Anxiety neurosis		1	1	5
Conversion reaction	2	0	1	1
Personality disorders				
Adolescent behavior problem	1	0	0	1
Impotency	1	0	0	1
Chronic brain disorders				
Cerebral arteriosclerosis	2	0	1	1
	101	13	36	52

ic patients treated, 11 (59.9%) showed definite improvement.

Side-Effects

The most frequent side-effects reported were lethargy (16%), pseudo-Parkinsonism (12%), and dizziness (5%), with blurred vision, dryness of mouth, lactation, stress incontinence, headache, dermatitis, and increased dreams developing in one case each. Pseudo-Parkinsonism was characterized by muscle tension, tremor, and considerable secondary anxiety, with some patients showing rather peculiar responses, such as localized increased tonus of the anterior neck muscles with difficult jaw occlusion, involuntary rigidity of the antigravity muscles, coarse periorbital tremors, mask facies, and propulsive gait. Patients with pseudo-Parkinsonism response exhibited the symptoms rapidly; the symptoms recurred each time the drug was reintroduced, and they rapidly subsided with discontinuation of drug therapy. Approximately the same number of patients developed subjective "side-effects" on placebo as on drug.

While on the drug, 12% of the patients developed a polymorphonuclear leukocytosis with between 10,000 and 15,000 cells per cubic millimeter; 6% showed an eosinophilia; 3% showed a slight lymphocytosis, and 2% demonstrated a 1-point increase in cephalin flocculation. Other laboratory tests were within normal limits. Bodyweight recordings demonstrated a slight shift toward optimum for the patient's height and bone structure. Concurrent hypertension in four patients was not influenced by thiopropazate therapy, but five patients with initial high blood glucose levels shifted to lower levels on the drug.

Both the control marrow biopsies showed a mild normoblastic hyperplasia, and one showed a slight increase in plasma cells. Of the nine bone-marrow biopsies done after the patients were on the drug, five showed a slight normoblastic hyperplasia, three an increase in mature lymphocytes, one an increase in eosinophils and plasma cells, and another an increase in megakaryocytes.

Summary

Thiopropazate hydrochloride (Dartal) chemotherapy has been employed in the treatment of 104 psychiatric patients, the majority of whom were schizophrenics. The drug has a definite ataractic effect for both acute and chronic disturbances, and 77 patients (74% of the total group) showed some over-all improvement on the drug. The drug is particularly useful in treating patients with association defect, depersonalization, and anxiety; and, although the statistical significance of the drug effect is not as definitive, it also appears to be helpful in treating patients manifesting delusions, withdrawn sociability, flattened affect, and anorexia. Patients with mood depression do not respond to thiopropazate therapy and demonstrate greater improvement when taking placebo.

No serious side-effects were encountered, but the development of excitation and Parkinsonism-like symptoms in some patients produces considerable secondary anxiety, necessitating discontinuation of the medicine. No evidence of myeloid depression has been found. On a milligram basis, thiopropazate hydrochloride is about five times as potent as chlorpromazine (Thorazine), and the recommended dosage is 5 to 10 mg. four times a day.

The Guidance Center, 1737 Prytania St. (13).

The Stability of Epinephrine and Arterenol (Norepinephrine) in Plasma and Serum

A Comparison of Normal and Schizophrenic Subjects

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With the Technical Assistance of Patricia Doolin

Introduction

Hoffer and co-workers[1,2] have suggested that adrenochrome, an oxidized derivative of epinephrine, may be involved in the development of schizophrenia. In support of this thesis, Leach and Heath[3] presented data which they felt were indicative of the instability of epinephrine in the plasma of schizophrenic patients. In the studies of the latter authors, epinephrine (2 mg.) was added to 1 ml. of plasma or serum obtained from schizophrenic and normal subjects, and, at a later time, the extent of formation of an absorption band at 395 mμ was spectrophotometrically determined. In the schizophrenic group, the 395 mμ band was found to have developed, on the average, to more than twice the extent noted for the normal group. These data were interpreted as indicating a more rapid formation of an oxidized form of epinephrine in the schizophrenic group.

In the course of our own studies dealing with fluorometric determinations of epinephrine and arterenol (norepinephrine),[4,5] we were impressed with the remarkable stability of both these substances in human plasma. Therefore it was decided to repeat the Leach and Heath experiments, utilizing fluorometric analyses to measure directly the rate of disappearance of epinephrine and arterenol from plasma or serum. The data presented in this communication demonstrate the high degree of stability of both epinephrine and arterenol in normal serum and plasma, as well as the lack of any significant difference in stability between our normal and schizophrenic groups.

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Methods and Materials

1. *Subjects*.—The schizophrenic subjects were all hospitalized at the New York State Psychiatric Institute. The clinical diagnosis for each is listed in Table 2. The normal group of subjects consisted of personnel workers at the Columbia-Presbyterian Medical Center, New York. The two groups were of comparable ages.

2. *Analytical Technique*.—Epinephrine and arterenol were isolated from plasma or serum and subsequently converted into fluorescent derivatives, as described in detail elsewhere.[4,5] In short, the isolation technique consisted of absorption of the epinephrine and arterenol onto the surface of aluminum oxide, followed by elution with dilute acetic acid. Eluates were adjusted to pH 6.5 and then oxidized to adrenochrome and noradrenochrome by shaking with manganese dioxide. Subsequent addition of 5 N sodium hydroxide, containing L-ascorbic acid, resulted in rearrangement of adrenochrome and noradrenochrome to their corresponding fluorescent tautomers, adrenolutin and noradrenolutin; the presence of L-ascorbic acid prevented decomposition of the lutins. Fluorometric readings were obtained as described previously,[5] with a modified Farrand filter fluorometer and two sets of primary and secondary filters. Separate standards of 0.4μg. epinephrine and 0.4μg. arterenol, as well as a reagent blank, were prepared for each set of analyses. The epinephrine standard, when converted into its fluorescent lutin, was utilized to standardize the fluorometer.

3. *Experimental Procedure*.—Stock solutions of *l*-epinephrine (adrenaline) bitartrate (Winthrop-

Stearns) and levarterenol bitartrate monohydrate (Winthrop-Stearns) were prepared in 0.01 N HCl at concentrations of 1 mg. pyrocatecholamine per milliliter, and stored at 0 C. Dilutions of 1.0μg. to 2.0μg. per milliliter were prepared in distilled water for daily use.

Routinely, 20-40 ml. of peripheral venous blood was drawn from the antecubital vein of subjects into either dry or heparinized (heparin sodium U. S. P. [Liquaemin sodium], 1000 units per milliliter, Organon, Inc., Orange, N. J.) syringes, and subsequently transferred to 40 ml. centrifuge tubes. Plasma was obtained by centrifuging the heparinized specimens at 700 g for 15 minutes; serum was obtained from the nonheparinized specimens by first allowing them to clot at room temperature for 45-90 minutes and then centrifuging. Plasma or serum specimens were split into two or three aliquots of 3-8 ml. each and placed in 15 ml. centrifuge tubes. One aliquot of each group was set aside as a control. The other specimens were incubated with 0.4μg. epinephrine, arterenol, or a 50:50 mixture of the two, at 37±1 C for one or three hours, as noted in Tables 1 and 2. The control specimens were also incubated at 37 C; however, the addition of epinephrine and/or arterenol was withheld until just immediately preceding the addition of aluminum oxide for the isolation procedure. The loss of epinephrine and/or arterenol incurred by incubation at 37 C was calculated by comparing the fluorescence of each specimen with its control, and with standards of epinephrine and arterenol. The fluorescence of plasma or serum without added epinephrine or arterenol accounted for only 1% to 5% of the fluorescence of the controls; this background fluorescence did not enter into the calculation of the percentage of loss, which was based on the difference in fluorescence between the control and the incubated specimens. The one- or three-hour loss of each specimen was calculated for each of the two sets of filters employed for fluorometric readings, and the average reported in Tables 1 and 2. In several instances where the average percentage of loss was a small negative figure, i. e., a gain of 3% or less, the data were considered to be within the limits of precision of the analytical procedure, and hence regarded as a 0% loss. For these specimens, the three-hour loss was calculated by comparison with the fluorescence of the one-hour incubated specimens rather than the controls.

Results

The experimental results are tabulated in Tables 1 and 2. For the control group of normal subjects (Table 1), one-hour losses ranged from 0% to 9%, with an average loss of 2.5% (±3% a. d.), while three-hour losses ranged from 0% to 16%, with an average loss of 5% (±3% a. d.). For the schizophrenic group (Table 2), one-hour losses ranged from 0% to 8% (average, 3%±2.5% a. d.), and three-hour losses ranged from 0% to 11% (average, 4.5%±3% a. d.). No significant difference was detected between the two groups for either one-hour or three-hour incubation periods.

TABLE 1.—*Loss of Epinephrine and/or Arterenol Incurred by Incubation at 37 C in Plasma or Serum Obtained from Normal Subjects*

Subject	Sex	Specimen	Incubated Pyrocatecholamine *	Loss, % 1-Hr.	Loss, % 3-Hr.
1	M	P1	E & A	3	3
2 A	F	P1	E & A	0	8
B		P1	E & A	7.5	--
3	F	P1	E & A	0	2
4	F	P1	E & A	0	2.5
5	M	P1	E & A	0	1.5
6 A	M	P1	E & A	4.5	--
B		P1	E & A	8.5	--
7	F	P1	E & A	9	--
8	F	P1	E & A	0.5	--
9	M	S	E & A	0	--
10	M	S	E & A	0	--
11	M	S	E & A	0	--
12	M	S	E & A	6	6
13	M	S	E & A	--	0
14	M	P1	E & A	0	3
15	F	S	E	0	7
16	M	P1	E	3	16
17	M	S	E	--	7
18	M	S	A	--	4
19	M	S	A	0	3.5

Average 1-hr. loss = 2.5%±3% (a. d.)
Average 3-hr. loss = 5%±3% (a. d.)

* 0.4μg. of epinephrine (E), arterenol (A), or a 50:50 mixture of the two.

Comment

The main result of this investigation was that no difference could be detected between normal subjects and schizophrenic patients with regard to the stability of either epinephrine or arterenol in plasma or serum. Our finding was contrary to that of Leach and Heath, who presented data tending to support the thesis that epinephrine was relatively unstable in plasma or serum obtained from schizophrenic patients.[3] The

TABLE 2.—*Loss of Epinephrine and/or Arterenol Incurred by Incubation at 37 C in Plasma or Serum Obtained from Schizophrenic Patients*

Subject	Clinical Diagnosis	Sex	Specimen	Incubated Pyrocatecholamine *	Loss, % 1-Hr.	Loss, % 3-Hr.
1	Paranoid	M	PL	E & A	5	...
2	Paranoid	M	PL	E & A	6.5	...
3 A	Paranoid	F	S	E & A	5.5	...
B			PL	E & A	0	...
4 A	Paranoid	F	S	E & A	1.5	...
B			PL	E & A	8	...
5	Mixed, catatonic & paranoid features	F	PL	E & A	0	...
6	Mixed, catatonic & paranoid features	M	PL	E & A	3.5	9
7	Catatonic	F	S	E & A	...	2
8	Paranoid	M	PL	E & A	0	1.5
9	Paranoid	M	PL	E & A	...	0
10	Paranoid	M	PL	E & A	0	1
11	Paranoid	M	PL	E & A	3	8.5
12 A	Mixed, catatonic & paranoid features	M	PL	E & A	0	5.5
B			S	A	0	11
13	Paranoid	M	S	A	6	...
14	Paranoid	M	S	A	...	1.5
15	Mixed, hebephrenic & catatonic features	M	S	E	...	3.5
16	Catatonic	F	S	E	6	9
17	Paranoid	M	S	E	0	4

Average 1-hr. loss = 3% ± 2.5% (s. d.)
Average 3-hr. loss = 4.5% ± 3% (s. d.)

* 0.4 μg. of epinephrine (E), arterenol (A), or a 50:50 mixture of the two.

contradiction between the two sets of results deserves comment.

First, it should be noted that the analytical approach was different in the two investigations. We analyzed for epinephrine and arterenol directly and therefore obtained direct information concerning their rates of disappearance. Leach and Heath, on the other hand, measured neither the disappearance of epinephrine nor the formation of its oxidation product, adrenochrome, but, rather, the formation of a compound which absorbed light maximally at 395 mμ. The relationship between epinephrine and the compound absorbing at 395 mμ, as well as the correlation between the rate of oxidation of the former and the rate of formation of the latter, remains to be more fully clarified. Second, in a later publication [6] it was indicated that the formation of the 395 mμ absorption band could be partially inhibited by the preliminary ingestion of L-ascorbic acid by the subjects, and that hence observed differences among subjects might be due, in part, to dietary effects. Whatever the correct interpretation of the spectrophotometric data may be, our own reults demonstrate the strictly comparable stability of epinephrine (and of arterenol) in plasma or serum obtained from schizophrenic and normal subjects. In fact, the very stability of these pyrocatecholamines in human plasma in vitro makes it appear unlikely that circulating plasma could mediate the development of schizophrenia via the formation of metabolites of epinephrine and arterenol. For instance, it should be noted that only small losses of 9% or less could be detected after incubation for one hour at 37 C (Tables 1 and 2). In comparison, it has been demonstrated [7] that a single passage through the liver is sufficient to clear blood of its plasma content of epinephrine and arterenol. Thus the rate of enzymatic destruction of these substances in plasma is many orders of magnitude less than their over-all rate of disappearance from circulating plasma in vivo, and hence the rate of formation of metabolites of epinephrine or arterenol by plasma enzyme systems is of highly questionable significance.

Summary

Epinephrine and arterenol (norepinephrine) were found to be highly stable when incubated in human plasma or serum at 37 C. No difference in stability could be detected between specimens obtained from normal and from schizophrenic subjects.

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Current Status of the Funkenstein Test

A Review of the Literature Through December, 1957

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In 1948 Funkenstein, Greenblatt, and Solomon[12] reported a relationship between the blood pressure responses to injected epinephrine and methacholine and the clinical course in a group of psychiatric patients. Since this time, numerous reports have appeared concerning the procedures employed by these authors. Great variation exists in the technique of what has become popularly known as the Funkenstein test, and much of the data is contradictory. It is the purpose of this paper to consider the current status of the test with respect to the following factors, as reported in the literature: (1) test procedure and scoring; (2) reproducibility (reliability); (3) relation to psychiatric state, including (*a*) ability to predict response to psychiatric treatment, and (*b*) ability to serve as an objective indicator of psychological change; (4) implicit and explicit physiological assumptions, and (5) diverse applications.

I. Procedure and Scoring

A. Procedure.—As originally described,[12] the test was performed as follows: With the patient in "basal condition" and recumbent, blood pressure determinations were carried out until the systolic pressure was constant for a period of at least five minutes. On the first day, 1 cc. of isotonic saline was injected intravenously, and the systolic pressure followed until it returned to the base line. On the second day 0.05 mg. of synthetic *l*-epinephrine was injected intravenously and the systolic pressure followed by frequent auscultatory determinations (several per minute) until it returned to the base line. On the third day 10 mg. of methacholine chloride was injected intramuscularly and the blood pressure followed first at half-minute, then at one-minute, intervals, for a period of 25 minutes. This technique has been retained by the authors with the following modifications:

1. Since 1952[19] they have used 0.025 mg. of epinephrine.

2. In hypertensive subjects (systolic pressure >140 mm.) epinephrine was omitted and methacholine alone was given as above.[18]

3. In the past few years both drugs have been administered on the same day, with the methacholine injected 20 minutes after the blood pressure returned to the preepinephrine (basal) level. If severe anxiety is precipitated by the epinephrine, methacholine is deferred until the following day.[23]

Other investigators have independently modified the procedure; some have given both drugs on the same day, with epinephrine preceding methacholine[2,35,42,52]; others have given both drugs on the same day but with the order reversed[52]; and many have omitted epinephrine and given only methacholine.[5,9,10,36,40,45,49,51,56,58] Laane[37] used a commercial preparation of epinephrine and administered the drugs on separate days, but with methacholine given first.

B. Scoring.—Initially, Funkenstein et al.[12] separated their patients into seven groups on the basis of the systolic blood pressure response. The criteria for each group are listed in Table 1. The data may also be described graphically; blood pressure is plotted on the ordinate against time,

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TABLE 1.—*Funkenstein Criteria for Classifying Responses to Injected Epinephrine and Methacholine*

	Blood Pressure Group						
	1	2*	3*	4	5	6	7
Response of systolic BP to intravenous injection of 0.05 mg. synthetic epinephrine †	Rise > 50 mm.	> 75 mm.	Rise > 50 mm. < 75	Rise > 50 mm.	Rise < 50 mm.	Rise > 50 mm.	Any reaction
Response of systolic BP to intramuscular injection of 10 mg. of methacholine chloride	Minimal fall in systolic BP which then rises above the control level, failing to return to this level within 25 min.	Moderate or slight fall in systolic BP; secondary rise may be present, but control level is reached within 25 min.	Same as Group 2	Moderate fall in systolic B P with marked secondary rise; control level reached for at least 3-5 min. within 25 min.	Fall in systolic B P with failure to regain control level within 25 min.	Same as Group 5	Includes all cases in which a chill occurs; BP could not be reliably determined ‡

* These groups were later combined into a single group 2-3.

† Smaller rises are accepted throughout if 0.025 mg. is injected (cf. Sloane and Lewis [53]).

‡ Sloane and Lewis were able to record blood pressure during chill and found that the resulting methacholine curve was distributed throughout groups 1-6.

on the abscissa. Figure 1 describes a number of quantitative measures which may be derived from such a graph; these include the height and duration of the blood pressure rise following epinephrine, the degree and duration of fall in response to methacholine, and the area under this latter curve. Occasionally, the methacholine curve is diphasic, with an initial fall and then a secondary rise in pressure after the base line has been reached. In such cases the secondary rise may be scored by subtracting the area under its curve from that under the curve described by the fall (Funkenstein et al.[19]) or by treating it as a separate variable (Sloane et al.[52-54]). Measurements of area are more laborious than grouping. Such measurements have been carried out by the above investigators and, in addition, have been reported by Elmadjian et al.[9,10] Manger et al.[40] Hirschstein,[35] Weckowicz,[56] and Nelson and Gellhorn.[44]

Other investigators have adhered to the Funkenstein groupings described above, or else have utilized the alternative grouping scheme suggested by Gellhorn.[25,28] This classifies the reaction to methacholine alone as being "normal," "hyperreactive," or "hyporeactive." Typical curves are shown in

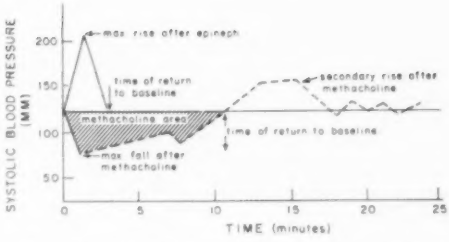

Fig. 1.—Quantitative measures derived from graphic representation of responses to epinephrine and methacholine.

Figure 2. Simon and Hopkins,[51] Schneider,[49] Jones,[36] Blumberg et al.,[5] Moriarity, in part,[43] and Stemmermann and Owen[55] have scored responses in these terms.

As noted above, Funkenstein et al.[18] modified the test for hypertensive patients by omitting epinephrine and injecting only methacholine. Patients were scored as Group A if their systolic blood pressure failed to regain the control level (i. e., "achieve homeostasis") within a 25-minute observation period, and as Group B if this level was reached within 25 minutes after injection.

All methods of scoring involve determinations of a basal systolic level and the

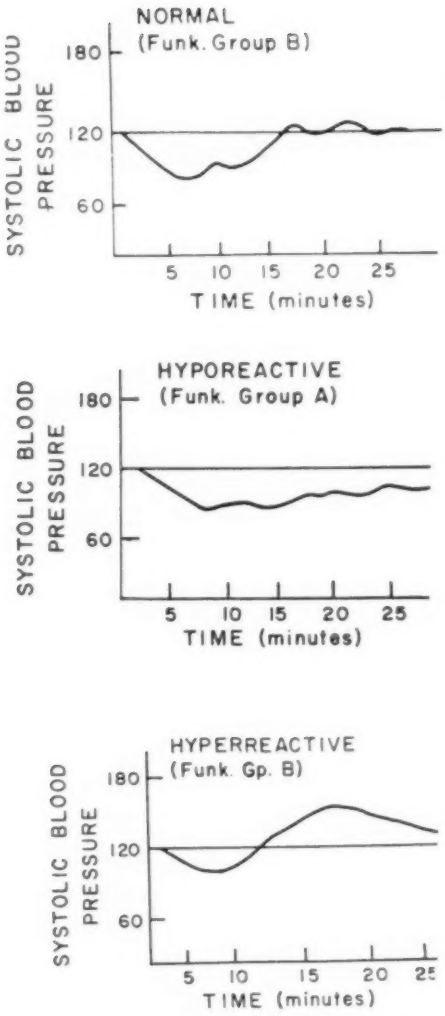

Fig. 2.—Idealized curves depicting the normal (upper), hyperactive (middle), and hyperreactive (lower) response to methacholine described by Gellhorn[20]; the corresponding categories used by Funkenstein et al.[19] to score the response of hypertensive patients to methacholine are also noted.

description of the duration and extent of drug-induced deviation from this level. With one exception, all investigators have apparently accepted the mean systolic pressure obtained in pretest readings as the basal level: Sloane and Lewis[52] have preferred a basal range extending ±8 mm. from the mean of determinations in a three-minute control period. Sloane et al.[52,53] also state their criterion for return to basal level; the standard adopted by other workers has not been explicitly stated.

II. Reliability and Control Groups

A. Reliability.—Reliability may be considered as the degree to which repetition of the test on a given subject, under conditions identical with those originally present, and with no change in clinical condition, will yield the same results as those initially observed. Using this definition, the evidence of reliability adduced by Funkenstein et al.[19] must be rejected, since it shows only that if the test is administered to two *different* large groups of patients, the distribution of cases found in each blood pressure group is not significantly different.

Three other studies are concerned with the reliability of this test. Weckowicz[56] administered methacholine alone to 20 psychiatric patients in the morning and evening of the same day. Rank-difference correlations between morning and evening tests were computed for areas under the blood pressure curves. Correlations of 0.90 for the fall in pressure and 0.82 for the rise above the base line were obtained. The results of 5 of the 20 patients tested were omitted from the statistical comparison because they reacted differently in the morning than in the evening. Had these results been included, the correlations would have been lower.

Sloane, Lewis, and Slater[54] reported the most complete study of test-retest reliability. They compared results obtained in 111 psychiatric inpatients in various diagnostic categories. The subjects were not tested during any somatic therapy; the retests were conducted within one week, and the authors were careful to exclude from comparison any patients whose clinical condition had changed during the interval. The results under various conditions of administration were compared with correlation measures for continuous variables (e. g.,

TABLE 2.—*Summary, in Part, of Reliability Data Reported by Sloane, Lewis, and Slater* *

Drug	Dose, Mg.	Technique	No. of Test-Retest Comparisons †	Concordance of Grouping	Concordance Prognostic Predictions	Test-Retest Correlations: Methachol. Area, Units	Test-Retest Correlations: Maximum Epinephrine Rise, Mm.
Epinephrine Methacholine	0.025 10	Epinephrine preceding Methacholine on one day	17	59%	71%	0.648	0.404
Epinephrine Methacholine	0.025 10	Methacholine preceding epinephrine on one day	11	90%	100%	0.334	0.346
Epinephrine (4 cases) (3 cases) Methacholine	0.05 0.25 10	Epinephrine preceding Methacholine on separate days	7	100%	100%	0.791	0.637

* Compare Figure 2.

† It is not stated whether more than one of these comparisons was performed on the same subject or whether, instead, each comparison represents data from a single subject. The former condition would tend to elevate the observed values.

maximum rise and fall, areas under curves, time to return to base line), and with per cent concordance for discontinuous variables (Funkenstein blood pressure groups and prognostic category). Their results are summarized in part in Table 2. It will be seen that the test is of low reliability if methacholine is administered after epinephrine on the same day, but that it is of adequate reliability for clinical use if this order of administration is reversed or if the drugs are given on separate days. The correlations are generally low but positive; those listed for separate-day administration for the height of blood pressure rise after epinephrine and for the area of fall after methacholine are among the highest obtained. Sloane et al.[34] also noted that results were more similar when both test and retest were conducted by the same observer and that administration of 0.05 mg., rather than 0.025 mg., of epinephrine yielded more reliable results. However, when epinephrine preceded methacholine on the same day, the larger dose reduced reliability even more than did the smaller.

Lotsof and Yobst[38] investigated the reliability of the Funkenstein test in 30 psychiatric patients, half of whom were tested in the morning and half in the evening; 15 medical students were controls. Although they administered *both* epinephrine and methacholine (on separate days), they did not describe the reliability of Funkenstein blood pressure groups and reported only product-moment correlations. Their study fails to indicate in some instances precisely what was being correlated, and they apply Funkenstein's scoring scheme for hypertensive patients to subjects with normal blood pressure. The correlations they report for continuous variables are of the same order of magnitude as those noted earlier by Sloane et al.[34]

B. Control Groups.—There are few published data describing the response of normals to the complete Funkenstein test, in which epinephrine and methacholine are administered on separate days. Funkenstein et al.[14] describe results in 15 subjects, 10 of whom were medical students. The mean age of these subjects was 23 years, presumably less than that of the experimental (patient) group studied. The majority of these subjects (80%) fell into Groups 2-3. Sloane and Lewis[32] reported results in 12 controls, finding a distribution similar to that of Funkenstein. They did not specify the age of these subjects. Lotsof and Yobst[38] administered the complete test to 15 medical students but did not report the results in terms of Funkenstein groupings; they also failed to present age data for these subjects.

Nelson and Gellhorn[44] administered methacholine alone to 104 normals and 236 psychiatric patients. They measured the area under the methacholine curve planimetrically and established three arbitrary groups: Group I (hyperreactors), Group II (intermediate), and Group III (hyporeactors). They found that a hypotensive effect was greater with increasing age in both normals and patients, and that this correlation was present even when the groups were matched for resting systolic pressure. When older subjects with elevated blood pressure were included, the hypotensive effect was still more pronounced. This work corroborates the earlier results of Blumberg et al.[5] and Lotsof and Yobst[39] in psychiatric patients, and of Clemens[8] in patients hospitalized with neoplasms. Such findings require that the effect of age on the complete Funkenstein test be evaluated.

III. Validity of Funkenstein Test as Index to Psychiatric State

The Funkenstein test has been utilized as an objective physiological index of clinical change in psychiatric patients and as a means of predicting the response of such patients to psychiatric treatment. Although the earliest publications were concerned with the relationship of blood pressure response to clinical state, it is the latter aspect of the test, its value as a prognostic instrument, which received most attention, and which therefore will be described first.

A. Prognostic Validity of Test.—In 1952, Funkenstein et al.[19] summarized their experience with use of the test for predicting response to electroconvulsive therapy (ECT). They classified psychiatric patients as improved if they could be discharged from the hospital within one month of their last shock treatment without requiring any other somatic therapy, and if they were able to remain out of the hospital for at least one month after discharge. As may be seen in Table 3, they found a striking relationship between this criterion of improvement and test responses which placed patients in Groups 6 and 7. Patients in Groups 1-5 responded much more poorly than those in Groups 6 and 7; consequently, the former may be termed "unfavorable" and the latter "favorable" groups (Table 4). Anxiety induced by injection of epinephrine, although not in itself as ominous a prognostic sign as was noted in an earlier study,[16] still appeared to worsen the prog-

TABLE 3.—*Data Obtained in Three Prognostic Studies of the Funkenstein Test*

	1	2 3	4	5	6	7
Funkenstein, Greenblatt, & Solomon [17]						
N=259						
No. of patients in BP group	32	85	11	10	89	32
% total sample in BP group	12.4	32.8	4.2	3.9	34.4	12.0
No. improved in BP group	3	30	1	1	79	31
% improved in BP group	9.4	35.3	9.1	10	88.8	96.9
Alexander [1]						
N=201						
No. of patients in BP group	8	63	22	10	95	2
% total sample in BP group	4.0	31.3	10.9	4.9	47.8	0.99
No. improved in BP group	6	32	13	2	68	1
% improved in BP group	75.0	50.8	59.0	20.0	71.0	50
Sloane and Lewis [43]						
N=111						
No. of patients in BP group	4	57	17	10	16	7
% total sample in BP group	3.6	51.4	15.3	9.0	14.4	6.3
No. improved in BP group	2	36	9	3	10	3
% improved in BP group	50	63.2	52.9	30.0	62.5	42.9

TABLE 4.—*Summary of Data Listed in Table 3 by "Unfavorable" (BP Groups 1-5) and "Favorable" (BP Groups 6-7) Prognostic Groups*

	Unfavorable 1-5	Favorable 6-7
Funkenstein, Greenblatt, and Solomon		
No. in BP group	138	121
% of sample in BP group	53.3	46.7
No. improved in BP group	35	110
% improved in BP group	25.4	90.9
Alexander		
No. in BP group	103	98
% of sample in BP group	51.2	48.8
No. improved in BP group	53	69
% improved in BP group	51.5	70.4
Sloane and Lewis		
No. in BP group	88	23
% of sample in BP group	79.3	20.7
No. of improved in BP group	50	13
% improved in BP group	45.0	11.7

nosis significantly. Anxiety induced by methacholine was again noted to be a favorable sign. Data from two other studies of the prognostic value of the test which employ Funkenstein's scoring scheme, and which involve comparable numbers of subjects, are included in Tables 3 and 4. It will be seen that Alexander's[2] results corroborate the general trend observed by Funkenstein, but certain discrepancies are apparent when the data are analyzed for individual groups. Thus, Group I (Table 3), the worst prognostic category in Funkenstein's series, shows the highest level of improvement in Alexander's study.

Sloane and Lewis[52] were unable to confirm any of the major findings of Funkenstein. In their study of 111 psychiatric patients treated with ECT and scored by the same criterion of improvement as that adopted by Funkenstein, they found no correspondence between "favorable" blood pressure response categories and improvement. They found also that methacholine-induced anxiety, as well as that caused by epinephrine, appeared to worsen the prognosis. The nature of the populations studied, therapeutic procedures, criteria of improvement, and over-all level of improvement found are listed in Table 5. It will be noted that Sloane and Lewis have duplicated the original Funkenstein study in almost all major respects* except in their use (in a majority of their subjects) of the one-day test with the epinephrine preceding methacholine. Sloane, Lewis, and

* Funkenstein[29] has stressed the difficulty of duplicating today the kind of acutely ill mental hospital population prevailing 10 years ago. He feels that the widespread use of psychotherapy, drug therapy, and electroshock therapy has made possible successful outpatient treatment for many patients who formerly would have been hospitalized. The patients now reaching the hospital are, in the great majority, those who have not responded to such treatments and therefore constitute a more severely ill population. Future prognostic studies would need to take this possibility into acount.

TABLE 5.—*Conditions of Studies Whose Data are Summarized in Tables 3 and 4*

Investigator	No. of Subjects	Patient Population	Test Conditions	Method of Treatment	Criterion of Improvement	Over-All Per Cent Improvement
Funkenstein, et al.	259	All diagnostic categories; inpatients, acute admissions	Two-day test; 0.05 mg. epinephrine	ECT (Reiter)	Discharge within 1 mo. of last ECT treatment; remains out of hospital at least one month	55.9
Alexander	201	All diagnostic categories; all acutely ill, approximately 2/3 hospitalized	One-day test; 0.025 mg. epinephrine	ECT (112) Psychotherapy (59) Insulin (24) Others	Social recovery with or without insight	60.7
Sloane and Lewis	111	As in Funkenstein series	One-day test (80) Two-day test (31) 0.025 mg. epinephrine	ECT (Strauss-MacPhail)	As in Funkenstein series	56.8

Slater [24] have reported that results of the one-day test are less reliable than those obtained when the two drugs are injected on separate days. This may account for the discrepancies between their results and those of Funkenstein. However, Funkenstein [23] and Alexander [4] state that the one-day and the two-day test appear of equal prognostic value. It should also be noted that results in the smaller number of patients, to whom Sloane et al. administered the two-day test, showed no trend in the direction predicted by Funkenstein.

Funkenstein et al.[18] modified the test for patients with hypertension (systolic pressure in excess of 140 mm.) by omission of epinephrine. The response to intramuscular administration of 10 mg. of methacholine chloride was scored as Group A if the blood pressure failed to return to the base line level within 25 minutes after an initial fall, and as Group B if this level was regained within this period. They found that Group A patients showed significantly greater improvement than did patients in Group B. Improvement occurred in 92.9% of the Group A patients, as contrasted with only 14.3% of Group B. This test has not yet been repeated in hypertensive patients. Sloane and Lewis [52] began such a study but were discouraged by the profound hypotensive responses they encountered. This observation, together with the large proportion of Group A reactions found in Funkenstein's series (two-thirds of their sample of 63), suggests that an initially elevated systolic pressure may be associated with a more pronounced hypotensive reaction to methacholine, a finding later reported by Nelson and Gellhorn.[44]

Other investigators have administered methacholine *alone* to *normotensive* patients. They have scored results as "normal, hyporeactive, and hyperreactive" according to a scheme put forward by Gellhorn. In evaluating these studies, it must be borne in mind that such scoring tends to combine Funkenstein's Group 5 with his Group 6 patients (Table 1). Since Group 5 was initially noted to have a poor prognosis, in contrast to the favorable prognosis of Group 6, pooling these patients in the same group is likely to blur prognostic discrimination if the original results are valid. Further, hypo- and hyperreactive patterns occur in normals,[44] and there is no reason to believe that emotional health is specially related to any particular pattern.

Blumberg et al.[5] found a relationship between greater hypotensive response to methacholine and improvement with ECT. However, they noted that hypotensive response to this drug also correlated markedly with age. They raised the possibility that correlations obtained between Funkenstein test results and response to therapy might represent merely the difference in distributions of psychiatric illnesses, with their differing prognoses, at various age levels. Table 6 lists the number and per cent of first admissions to United States mental hospitals by age and ECT-favorable and ECT-unfavorable diagnostic categories, as these are clinically defined. It will be seen that above the age of 45 there is a marked increase in the proportion of patients in ECT-favorable diagnostic categories. Since pronounced hypotensive

TABLE 6.—*First Admissions to Public Prolonged Care Hospitals for Mental Disease by Age and ECT-Favorable Groups* *

Category	15-24	25-34	35-44	45-54	55-64
No. patients in combined groups †	4518	9346	7885	5886	3255
% in ECT-favorable group (includes involutional psychotic reaction, manic-depressive reaction, and psychotic depressive reactions)	6.0	8.2	18.8	44.2	60.2
% in ECT-unfavorable groups (includes all schizophrenic and paranoid reactions)	94.0	91.8	81.2	55.8	39.8

* United States 1954, based on reports from 179 of 216 state and 47 of the 127 county hospitals.

† From "Patients in Mental Institutions," 1954, U. S. Public Health Service Publication, No. 523, Pt. II, Adapted from Table 5, p. 20.

("favorable") reactions also occur more frequently with advancing age, this alone may account for the prognostic value of the test.

Lotsof and Yobst[39] found that of 45 patients treated with ECT, there was no difference in response to methacholine between those who improved, as determined by Funkenstein's criteria, and those who remained unimproved. They also failed to find any relationship between methacholine response and improvement with therapy other than ECT.

Other studies bearing on the prognostic value of the test include those of Moriarity,[43] who found a correlation between *hyperreactive* pattern in response to methacholine and *improvement* with CO_2 therapy †; Simon and Hopkins,[51] who failed to find such a correlation, and Pasquarelli et al.[45] who found a positive relationship among good affect (judged clinically), hypotensive response to methacholine, and improvement in a series of psychiatric inpatients. Hirschstein[35] evaluated the ability of the one-day test (epinephrine preceding methacholine) to predict spontaneous improvement in a group of hospitalized, acute, first-admission schizophrenics. He found a significant correlation ($\rho = 0.43$) between blood pressure fall after methacholine and spontaneous improvement, as measured by the Gardner Behavior Chart. He also found a slightly higher correlation between a measure described as greater fall than rise in pressure after methacholine and discharge from the hospital within five months of testing. Geocaris and Kooiker[32] reasoned that among a group of chronic schizophrenics with clinically poor prognosis there should be few who fall into the favorable blood pressure groups. They administered the two-day test and found none of 25 such patients in favorable groups. However, there are as yet no data on the effect of prolonged, nonpsychiatric hospitalization on response to these drugs. Montagu and Davies[42] found no correlation between results on the one-day test, including the presence or absence of epinephrine-precipitated anxiety, and improvement of patients with anxiety neurosis who were treated with subconvulsive electrostimulation. They found this treatment itself no more effective than thiopental (Pentothal) placebo.

B. Value of Funkenstein Test as Objective Index of Clinical Change.—Funkenstein and others have published several studies[12 17] to show that the test responses of a patient change with his clinical condition. In an early study[14] they noted that, while test responses cut across diagnostic lines, there was a tendency for patients diagnosed as psychopathic personalities to fall into Groups 1 and 2, for neurotics to fall into Group 4, for schizophrenics to fall into Group 5, and for patients with involutional depressions to respond as Groups 6 and 7. Involutional depressions were most consistent in this respect. Twelve of their fifteen normals fell into Groups 2 and 3. In a second study published during the same year, Funkenstein et al.[15] noted that when clinical improvement occurred, the physiological response to the test approached the normal; these changes were in the direction of lower resting systolic pressure, increased pressor effect of epinephrine, and decreased hypotensive reaction to methacholine. Patients who responded to methacholine with anxiety or chill before treatment no longer manifested these responses after clinical improvement. Illustrative case histories demonstrating these changes were reported in a separate paper,[17] and it was stated

† A positive relationship between hyperreactive pattern and response to CO_2 treatment is postulated by Gellhorn[27 28] on the basis of his belief that such a pattern signifies increased hypothalamic activity (Sec. IV B). He suggests that CO_2 therapy reduces the increased activity of the hypothalamic center and thereby produces a remission of symptoms. However, hyperreactive patterns are found with greatest frequency among Funkenstein's unfavorable groups, and Funkenstein asserts[21] that their prognosis for improvement is poor with *any* therapy. These contradictory statements have not yet been reconciled.

that any significant alteration in the patient's psychological state is invariably accompanied by a change in his physiological response to the test.

This assertion has not been systematically studied by other investigators. Brothers and Bennett[6] noted that they found it to be true in every case; their study, however, was concerned mainly with the use of the test to choose method of therapy, and they do not present data which relate clinical change to test response. Jones[36] and Blumberg et al.[5] noted that they were unable to confirm such a relationship, but their studies were also primarily concerned with other aspects of the test. Stemmermann and Owen[55] administered the one-day test serially to psychiatric patients, examining 125 patients a total of 350 times. The major part of their investigation was concerned with the responses of 51 consecutive admissions to the psychiatric clinic, who were tested 237 times. Although both drugs were given, the authors found it advisable to utilize Gellhorn's scoring system, since the response to epinephrine was quite variable during ECT. They found a marked correspondence between the independent clinical estimate of the patient's progress and the methacholine response; if the pattern shifted in the direction of "normality," this was accompanied by a partial remission of symptoms. Of 186 such comparisons, there was complete agreement in 143 (77%), partial agreement in 41 (22%), and disagreement in only 2 (1%). It is not stated how many different patients were assessed in this manner. The degree of agreement obtained is remarkable in view of the generally recognized lack of reliability of clinical judgments and the markedly reduced reliability of the methacholine response when it follows the injection of epinephrine.

IV. Physiological Implications

It is probably reasonable to assume that the blood pressure effects of epinephrine and methacholine initially represent the effects of the drugs on peripheral end-organs and are independent of their effects on higher centers. Under this assumption, some of the variables involved in the observed response are (*a*) end-organ responsivity (adrenergic and cholinergic tissue), (*b*) receptor sensitivity (to the blood pressure changes), (*c*) the state of the CNS regulatory mechanisms, and (*d*) the response of various organs to the CNS output. While it may be possible to distinguish the contribution of these and perhaps other variables to the observed response, such studies have not yet been done. Therefore, it is possible that identical responses observed in different patients are the result of quite disparate mechanisms, and it is an oversimplification to regard these merely as "sympathetic" or "parasympathetic" tests. Clemens approached this problem by attempting to correlate the blood pressure changes after epinephrine[7] and methacholine[8] with known measures of sympathetic and parasympathetic activity, respectively. He found, in subjects hospitalized with malignant neoplasms, that the rise in blood pressure following epinephrine correlated well with sympathetic activity, but that the fall in blood pressure following methacholine did not furnish a good index of over-all parasympathetic response. One must be cautious in applying these findings to Funkenstein's data because the populations were markedly different, the route of administration of epinephrine was intramuscular rather than intravenous, and the dose of methacholine used was 5 instead of 10 mg.

A. Funkenstein's Interpretation.—Originally, Funkenstein et al.[15] considered the test a measure of "basal sympathetic tone," but in 1952[18] they first proposed the theory that variation in response to methacholine was dependent upon the relative circulating concentrations of epinephrine-like and arterenol-like substances. They suggested that the elevated blood pressure observed in their hypertensive series was in part the re-

sult of the stress of mental illness.‡ They demonstrated that Group A patients, whose blood pressure did not return to the base line within 25 minutes after injection of methacholine, differed from Group B patients in certain related measures. The area under the methacholine curve, and the maximal fall in blood pressure were significantly greater in Group A patients, and this led them to believe that Groups A and B represented two distinct populations. They postulated that the initially elevated blood pressure in Group A patients resulted from increased secretion of epinephrine in response to emotional stress, and that the hypertension in Group B patients resulted from increased arterenol secretion.§ Group A patients, then, were predominantly epinephrine secretors, and had a marked hypotensive reaction to methacholine and a favorable prognosis for ECT treatment; Group B patients secreted proportionately more arterenol, had a minimal hypotensive reaction to methacholine, and responded poorly to ECT. Some additional observations have been adduced to support this hypothesis:

1. In 10 healthy young normotensives the blood pressure was elevated by intravenous infusion of epinephrine and arterenol.[20] When methacholine was injected during administration of epinephrine, the hypotensive effect was marked, resembling that seen in the Group A patients; when the same drug was injected during infusion of arterenol, a minimal hypotensive effect, similar to that observed in Group B patients, was noted. However, this difference would be anticipated no matter what the hypotensive agent administered, and may simply reflect the more powerful pressor action of arterenol.

2. Elmadjian et al.[9] investigated the urinary excretion of pyrocatechol amines, as measured by bioassay after injection of insulin and methacholine. They found that 10 mg. of the latter drug caused a slight increase in arterenol secretion with no appreciable change in epinephrine. Elmadjian and his co-workers demonstrated in a later study[10] a significant negative correlation ($r = -0.51$) between the log of the methacholine area and arterenol excretion in a group of 10 normals, 11 chronic schizophrenics, and 4 acute schizophrenics. The normals showed no consistent relationship between epinephrine excretion and area, but the patients were found to have a significant positive correlation ($r = 0.63$) between log of methacholine area and epinephrine excretion during the test. These findings are in the direction predicted by Funkenstein. A correlation between the ratio of epinephrine-arterenol and degree of methacholine hypotension is implied by Funkenstein's theory and would have been of special interest; however, this has not yet been reported. An unexpected finding in this group of schizophrenics was a significantly greater fall in systolic blood pressure after methacholine than that found in the 10 normal controls. This again raises the question of the effects of prolonged hospitalization.

While the above work is consistent with Funkenstein's hypothesis that variations in methacholine-induced hypotension reflect the relative circulating concentrations of epi-

‡ In a later paper, Funkenstein and Meade[20] considered the possibility that the observed hypertension might reflect the greater age of this group rather than the stress of mental illness. They therefore determined the blood pressure after completion of ECT, in randomly selected patients from this series. They found that the mean blood pressure of these subjects was within normal limits, despite the fact that the mean age was significantly greater than that of the larger psychiatric group, from which these patients were drawn. They therefore concluded that illness, rather than age, accounted for the hypertension. However, it is known that abnormally elevated blood pressure tends to diminish with hospitalization alone.[11] Therefore, to demonstrate the effect of illness it is necessary to show that the blood pressure was reduced among patients who improved, and not among those who remained ill, despite an equal period of hospitalization for both groups.

§ This suggestion might be tested in part by measuring the diastolic pressure in such groups. In accordance with the known actions of the two drugs,[20] one would predict that the mean diastolic pressure in Group B would be significantly greater than that found in the patients in Group A.

nephrine and arterenol, that of Manger et al.[30] is not. They measured epinephrine-like and arterenol-like substances in the plasma of 21 subjects one to three and three to five minutes after the injection of 10 mg. of methacholine. Using the techniques of Weil-Malerbe and Bone and classifying the reaction to methacholine as normal, hyporeactive, and hyperreactive, they found "no indication that the type of blood pressure response was related to the concentrations of epinephrine and arterenol (norepinephrine) in the plasma." However, one does note in their data that among five psychotic patients, the hyporeactors showed a statistically significant per cent increase in epinephrine-like substance, and the hyperreactors showed a significant per cent decrease after methacholine. The nonpsychotic subjects showed no such relationship. This incidental finding is in the direction suggested by Funkenstein and might prove of heuristic value if established by further investigation. With the development of new and more specific techniques for assay of blood pyrocatechol amines, one may anticipate more definitive direct tests of the Funkenstein hypothesis.

Funkenstein and his co-workers[21,22] have attempted to relate affective responses of normals during stress (anger directed inward *vs.* anger directed outward) to relative secretion of epinephrine and arterenol. These imaginative and provocative studies are not directly relevant and therefore will not be discussed here.

B. Gellhorn's Interpretation.—Gellhorn et al.[25,26,28,31] and Redgate and Gellhorn[47,48] have interpreted the variations in blood pressure response to methacholine differently. They suggest that these variations reflect differing levels of hypothalamic irritability. This suggestion is based on the fact that the hypotensive reaction to methacholine in cats can be reduced by chemical and electrical stimulation in this area, and increased by the local injection of depressant drugs and by bilateral destructive lesions. There seems little doubt that such procedures do affect the methacholine response. However, one might expect that similar effects would be exerted by stimulation or depression of other areas, such as the cardiovascular centers in the medulla. Further, the work of Sigg[50] casts doubt upon the role of posterior hypothalamus as the critical factor in regulating the compensatory reaction to methacholine. He found that the hypotensive effect of methacholine was enhanced after acute bilateral electrocoagulation of the posterior hypothalamus, but that after a period of time (unspecified), despite these destructive lesions, the methacholine response returned to the normal (control) level. Even if the necessity of intact hypothalamic function for methacholine response were established in the surgically prepared, lightly anesthetized cat, one should hesitate to apply this finding to the fully conscious, intact human.

V. Other Uses of the Test

The Funkenstein test has had an extraordinarily wide variety of applications. Greenblatt, Funkenstein, and Solomon[34] found a relationship between blood pressure groups and response to lobotomy. Meadow and Funkenstein[41] reported that schizophrenics capable of abstract thinking were more frequently found in the favorable groups. Pasquarelli et al.[45] noted a correlation between "good" affect and favorable groups. Gellhorn,[25] Alexander,[1,3] Brothers and Bennett,[6] and Jones[38] have suggested that test response be utilized to decide the method of therapy. Sloane et al.,[53] although unable to confirm its prognostic validity, found that measures derived from the Funkenstein test differentiated among three diagnostic groups (neurosis, depression, and schizophrenia); however, as noted above, the factor of age was not controlled. Schneider,[49] accepting the validity of Gellhorn's interpretation of the test, used it to measure "central autonomic reactivity" and found in 10 patients that acute administration of reserpine and amobarbital (Amytal) affected the results. Vanderkamp et al.,[57]

in a brief note, suggest that "global" reactivity to methacholine is of prognostic value in patients undergoing insulin coma therapy. Zuidema et al.[58] have reported a relationship among high "g" tolerance, methacholine response, and arterenol-epinephrine excretion ratio in seven healthy normal subjects.

Many of the studies which report positive findings have not been sufficiently rigorous to permit definite conclusions to be drawn. The lack of systematic investigation of such findings is regrettable in view of the great theoretical and practical importance of the subject.

VI. Summary and Comment

1. The parameters of the Funkenstein test remain undefined, 10 years after the initial study. Control group data which adequately match the patient population for age are lacking. A pronounced hypotensive response to methacholine occurs more frequently in older persons and perhaps in those whose resting systolic blood pressure is abnormally high. The reliability of the response to methacholine appears reduced by previous administration of epinephrine. If the drugs are administered on separate days, or on the same day with methacholine given first, the test appears to be reproducible.

2. The demonstration by Funkenstein and his co-authors of a clear-cut relationship between blood pressure response to epinephrine and methacholine, and prognosis with ECT remains unconfirmed by independent investigation. While several studies cast doubt upon the original findings, these studies have differed sufficiently in their procedure as to leave the issue undecided. The possibility exists that a correlation between test response and prognosis may merely reflect the change in distribution of mental diseases which occurs with advancing age.

3. Until the contributions of age and initial blood pressure level to the observed response are more adequately assessed, it will be difficult to evaluate the operation of other physiological factors.

4. It is premature to use response to the Funkenstein test to determine choice of therapy for psychiatric patients.

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Ambiguity and Repression

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Introduction

In his paper on repression[11] Freud states that "the essence of repression lies simply in the function of rejecting and keeping something out of consciousness." This function is implemented in a number of ways. These differing ways complement and combine with one another to produce repression, but a few of them may be separately appraised in order to investigate their particular roles in the total process.

Repression Without Primary Psychological Content.—Here the subject may become aware of an *inability* to think about or approach a certain area of feeling. Sometimes, as in trying to remember a forgotten name, there is awareness of something which cannot be reached, or can be reached only partially. The feeling of the sound of the name, the number of syllables, the inflection in its pronunciation, may be felt before the actual word is recalled. In some active states of repression the mind feels *forced* away from a certain mental area in a way rather analogous to the repulsion exerted by like poles of magnets. Psychologically, content cannot be ascribed to this process by the subject. His mind may be blank, but the area of the blank cannot even be considered.

A patient with severe castration anxiety developed the very strong feeling that his penis was not there. He was unable to have a mental image of his penis. He tried to reassure himself by touching it. Still he was unable to feel that it was there. On trying to think of it, he felt a centripetal force, making it impossible to consider, though he could think of many other things. He summed it up as a feeling: "I am *unable* to think of it." The patient was having, in this experience of very active repression, a kind of awareness of neurophysiological functioning. The physical analogy that this process suggests (active repulsion) and the impossibility of representing it psychologically—that is, as idea, feeling, or image—lead me to infer that in this sort of repression we are dealing with the bare bones of neurophysiology. This is psychological awareness of neurological inhibition. It is analogous to a person contemplating an organically paralyzed limb. Trying to move it leads to a feeling of impotence. It has been lost from the realm of psychological processes. The metapsychological description of repression[12] as a process of withdrawal of preconscious cathexis from an idea, and the use of this cathexis as anticathexis to hold the idea out of the preconscious, is not a psychological description. It is a description of a hypothetical physiological process of changing distributions of excitation and inhibition and, motivated though it is by psychological elements, e. g., wishes, drives, ideas, and memories, per se it is without psychological content. This physiological quality of repression is referred to by Grinker,[13] who considers that repression in psychoanalysis and inhibition in neurology are dynamically identical. Alexander[1] refers to repression as a reflex inhibition functioning like conditioned reflexes. In therapy our attempt is to reconvert this neurophysiological process into a psychological one.

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Memories Used as Barriers Against the Emergence of the Repressed.—In these instances, which I have described at length elsewhere,[15] early memories of actual screens and barriers in the environment, e. g., the breast, mother's body, clothing, actually comprise, exist in, or are immanent in the "blankness" in the mind which denotes repression. Asking a patient to describe a state of mental blankness may produce vivid associations, frequently to the maternal breast, sometimes to articles of clothing, etc., which hide objects from view. Several other observers have since noted this phenomenon in their clinical experience.

My impression is that repression using actual memories of screens and barriers is not as active a process as the purely physiological one described above. The subject can attempt to look at, consider, investigate the state of blankness, and even penetrate it directly, as if it were a curtain, behind which lies the repressed content. Though the physiological substrate is here, to it has been added a psychological representation—a memory—which is subject to psychological analysis, and therefore produces less of the feeling of dealing with purely neurophysiological events.

Nonrecognition of Certain Aspects of Imagery

This process also plays a part in the function of keeping feelings and thoughts from consciousness.

In the course of some studies of psychosomatic disorders, patients were requested to make drawings of dreams or images. The subjects were then requested to look at their drawings and describe what they saw in the pictures. In several instances, rather striking reversals of content occurred. What had been originally drawn and seen in one way was now seen as its opposite.

Clinical Data

Case 1.—Miss A., a young woman with atopic dermatitis, was given a suggestion that she would dream. She dreamed that night of someone chasing or scaring her. She was asked to make a drawing of this, which she did (Fig. 1). She was then asked to look at her drawing, and she said that it now looked like her approaching her mother's casket, and her mother was lying in the casket. This patient had consciously entertained thoughts of her mother in a casket prior to her mother's death, three years before. She had never gotten on well with her mother and had been intensely rivalrous with her. Her brother said the patient's wild behavior had caused the mother's death.

Comment: Sexual interest and desire and sexual fear are represented in one view of the picture, someone chasing her; and the other side of the conflict, hostility and guilt toward the mother, is represented in *another way* of looking at the same picture—the patient approaching her mother's casket. The shift in this instance is accomplished by a change in assigning identities and roles to the figures in the drawing. The drawing is so constructed that this is easy to do.

Case 2.—A young man with severe atopic dermatitis was given a suggestion to dream. He had the following dream: "I was in the Navy—went some place in my car with a couple of buddies. We had girls with us, and went into a show. The other sailors were with girls, couples walking down the aisles. I don't know how I got separated from my buddies—but I didn't have a girl. Then, like an officer, I yelled for them to stop. I asked where my girl was. Somebody said my buddy had taken my girl. I got mad and went up the aisle, saluted an officer. I saw a buddy from my home town and sat with him. Then I went to my car."

The patient said the dream was silly. He'd been turned down by the Marines because of his eczema. If a buddy makes out better with a girl than he does, this only means the other man is a better

Figure 1

Figure 2

man than he. What he does in such a situation is go and look for someone else. The patient was then asked to try and make a drawing of the dream and, with much hesitation, did so (Fig. 2).

He described the drawing as of the people going down the aisles in the movie theater. Also, he could see people sitting along the aisles. The large figure to the left was himself, walking into the auditorium, down the aisle—the situation where he had become separated from his girl friend and his buddies. He was then asked to look at his drawing and tell his impressions of it. He first said: "It's just what I saw, that's all." Then he said: "Might be a stage, like vaudeville days, and this one [the large figure representing himself] might be the main actor; a singer waiting in the wings, or maybe the leader. Maybe the girls are dancing, and this fellow is back here singing. Maybe it is like a dance hall in the Westerns. The girls are dancing, and the fellows are watching them. Or maybe it is kids sitting at desks in a schoolroom, and the prof up there is looking down at his class, giving them a lecture. Or it is a graduation—fellows and girls walking down the aisles for diplomas, and the president of the school board is the main object in the picture, the important one."

Comment: The alternation between looking and being looked at is evident. The manifest content of the dream is of losing out, being inferior. On his looking at the same picture in another way, the patient's wishes to shine, be big, etc., are very clear. There has been a shift in the role of the subject. From being the inferior outside onlooker, he shifts to become the focus of attention. His large size in the picture shows the latent meaning, even though he is presented originally in an ostensibly and ostentatiously inferior position.

Case 3.—An adolescent boy with atopic dermatitis was requested to imagine something and make a drawing. His father was in the hospital at this time, recovering from a serious operation, and the boy had just been to see him. He drew the hospital room where his father was staying (Fig. 3). The picture showed the hospital beds, a television set, a table to eat off, etc. Asked to look at the picture, he said: "I think about dad a bit. He's not home. He's not having a bad time now; more or less cheerful. This is more

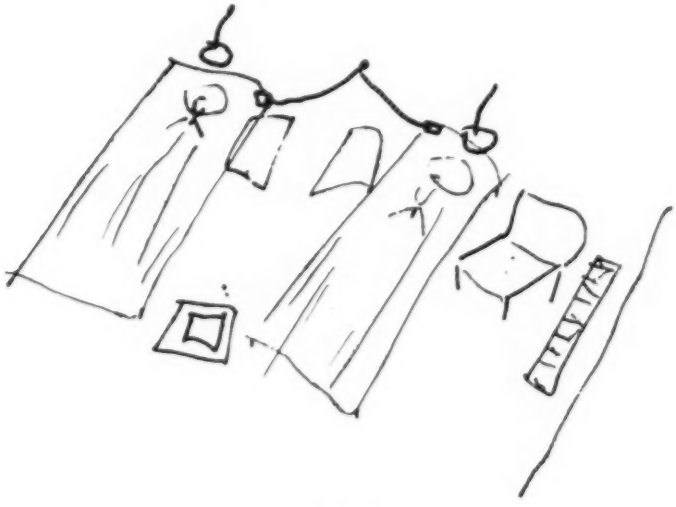

Figure 3

or less a happy room. He can answer the phone now. He's skinny—lost too much weight from the operation." He was asked if he got any other impression from the picture. "Looking at it sideways, it reminds me of a clothes closet with two people in cellophane bags hanging in the closet." He was asked about the people in the bags, and he said, trying to evade the question: "I just added this. It doesn't remind me of anything. Shall I see if I can get anything else out of the picture?" He was again asked about the people in the bags, and he then said: "Dead or something. A murder case, a crime. They put them out of the way, shoved them in cellophane bags, and zipped them up so that they wouldn't find them. There is something I ought to tell you. I always get my girl friend mad—get her mad because at times I drive real fast. I don't care then if I hit a phone pole. I feel miserable about my skin. It's not good, not cleared up. Being a pessimist is in me. Maybe I tell my girl friend these feelings so she'll feel sorry for me—just a way to get somebody to look at you, feel sorry for you."

Comment: The ambivalence toward his father, stirred up by the father's operation, emerges with considerable feeling on his looking at the picture (the bags with the murdered people=hospital beds) and then leads to guilt reactions of self-destruction and masochistic exhibitionism. The manifest content of the image is positive feeling toward father, the cheerful hospital room. The latent content is hostility toward the father. The shift from one attitude to the other parallels a shift in figure-ground relationships in the drawing. In the original way of looking at it, the man in the bed was figure, and the bed was background. On changing the viewpoint, the bed and the man in it all become figure—the man in the cellophane bag.

That drawings of dreams and images contain "buried figures," or have meanings other than those consciously intended, has been demonstrated before by Marcinowski[20] and by Fisher,[4] who has many fine examples of this type of drawing.

This way of looking at latent meanings may be readily applied in clinical practice. Patients frequently make statements which have one meaning if taken as they are intended, another if the latent content of the ambiguous statement is considered. A dream demonstrates this. A man dreams that cats jump on his leg, preventing him from leaving his home. The dream occurs at a time when he is experiencing anxiety at being separated from a beloved woman. He thinks the cats represent clawing women. He is asked how he might regard this dream differently, and he says that the cats remind him of children grabbing grown-up's legs to keep them from going out. The cats represent him as a clinging child. The dream is commonplace. What I wish to emphasize is that the image of the cats jumping on the subject is a reversible picture, like the drawings presented above. What makes possible the reversal from cats as clawing women to cats as himself as a clinging child is a change in attitude or way of looking at the dream image. This change is brought about by the process of directing his attention to the image, i. e., by the analytic work.

Conclusions from Clinical Material

1. Attitudes absent from the originally described (manifest) content of dreams or images are represented in drawings of the dream or images and appear when the drawing is looked at as a more or less external object.

2. That which is discovered on scanning the drawing is of meaning antithetical to the manifest content.

3. That which is scanned is a pictorial representation of a temporospatial Gestalt, the dream or image.

4. Antithetical reversals of this type abound in clinical psychoanalysis, and their occurrence is one means by which repression is overcome.*

* The application of conscious attention to preconscious trains of thought is described by Freud[8] as a prerequisite to their becoming conscious, so that what is overcome might be considered to be more in the nature of preconscious suppression than of dynamic repression. Actually, what emerges in the three instances cited varies from an already virtually conscious attitude, in the first subject, to preconscious attitudes, in the second subject, to ideas and feelings which have been subjected to a considerable degree of dynamic repression, in the third subject.

5. These reversals may occur in a number of ways. These include shifts in the identity of personages in the dream or image, changes in role, and changes in figure-field relationships altering the meaning of the original presentation.

These ambiguous images, the buried figures they contain, and their reversibility, may be considered from several standpoints.

Psychoanalysis: Ambiguity and multiple representations by the same image are extensively dealt with in the "Interpretation of Dreams,"[6] especially in Chapter VI, on the dream work. Freud points out that words, by their ambiguity, may express several dream thoughts. The same elements in a dream may be considered to have antithetical meanings. "The construction of collective and composite figures is one of the chief means by which condensation operates in dreams."[7] This condensation may be effected in several ways. One figure may represent others through having some attributes of another person (Irma dream). Or the actual features of two or more people may be fused into a single image. The dream of the uncle with the yellow beard[8] is an instance of the manner in which ambiguous images are formed.

> What I did was to adopt the procedure by means of which Galton produced family portraits; namely by projecting two images on a single plate, so that certain features common to both are emphasized, while those which fail to fit in with one another cancel one another out and are indistinct in the picture.[7] Dreams feel themselves at liberty moreover to represent any element by its wishful contrary; so that there is no way of deciding at first glance whether any element that admits of a contrary is present in the dream thoughts as a positive or negative." It is, indeed, not easy to form any conception of the abundance of the unconscious trains of thought, all striving to find expression, which are active in our minds. Nor is it easy to credit the skill shown by the dream-work in always hitting upon forms of expression that can bear several meanings—like the Little Tailor in the fairy story who hit seven flies at one blow.[9]

Thus, the dream work presents the perceptual system with ambiguous figures, capable of being seen in more than one way.†

Gestalt Psychology

The presentation of ambiguous figures to consciousness brings us to the province of Gestalt psychology. Ambiguous figures were first studied by Rubin, and their investigation was then taken up by Wertheimer and the Gestalt school.

Gestalt psychology emphasized that initial perceptions are of total configurations, or wholes, rather than being compounded by a central process from a large number of peripheral sensations. The tendency to perceive configurations results in a differentiation between figure, which is formed, highly articulated, possessing a high energy level (in Gestalt terms), and background, which is not articulated and is relatively formless. A figure is perceived and set off from the background as result of certain conditions, which have been carefully studied. These include the nature of its contours, closure, its "goodness" as a figure, its meaning, its "pregnancy," etc.

If an ambiguous figure is originally perceived in one way, there is a tendency for it to be so perceived on subsequent occasions; i. e., a set has been established. If a reversal of figure-ground relations occurs, the original field is not readily perceived. "What is recognized then is not the stimulus aggregate but the perceptual response which we call a figure."[28] The tendency to perceive an ambiguous figure in one way is conveniently illustrated by the famous "My Wife and My Mother-in-Law" drawing[2] (Fig. 4). This figure will be perceived either as a young woman or as an old woman. The experience of many people is that they are able to see only one person, until the other is pointed out to them. My

† Experiments by Fisher and others with tachistoscopic presentations of visual images indicate that registration of the visual stimulus occurs at preconscious levels, and then may be represented in drawings as a buried or ambiguous figure whose relationship to the original subthreshold stimulus may be recovered on inspection.

Figure 4

own experience was that I was unable to see the old woman, despite many efforts, until I read the following description by Perls.[23]

> This picture has been constructed so that various of its details have a dual function. The long promontory which is the old hag's nose is the whole cheek and jaw-line of the young woman. The hag's left eye is the young woman's left ear, her mouth the young woman's velvet neck band or choker, her right eye a bit of the young woman's nose, etc. If we could trace these for you, it would be more helpful, but by now you probably have seen the second picture. It will have come suddenly, perhaps startling you into a little exclamation of surprise. This is what the Gestalt psychologists call the "aha! experience."

Is the "aha! experience" upon being able to perceive the hidden face the equivalent of the effect of an interpretation overcoming a resistance? Certainly we regularly observe how persons stubbornly insist on seeing the same stimulus aggregate in one way, though to the analyst other ways of perceiving it are possible.

On the other hand, Köhler,[16] in discussing reversal in ambiguous figures, pointed out that prolonged occurrence of a figure process in a given area of the visual system leads to gradual changes in this area, a kind of satiation, which opposes the further existence of the process in the same place: [17] "In other words, a figure process seems to have some effect by which it tends more and more to block its own way." The organizing forces that maintain the process become weakened. Another example of this occurs when we repeat any word many times. The word then tends to lose its meaning and becomes meaningless sound.

Perhaps satiation of this sort results in loss of ability to organize a particular set of ideas or feelings, causing its dissolution, and replacement for a time by another mental state.

Ambiguous figures designed so that background and figure are dynamically interchangeable illustrate this (Fig. 5). If we look at the cross, we may see it as black, and then suddenly, and with no conscious intervening process, it will leap to white. As we continue to gaze, it changes back to black, and the alternation may continue for a long time. Shifts of this type are, I think, exact parallels of what happens when feelings and thoughts emerge from repression in analysis. The strength of the new and old figures are approximately equal, and there is an alternation back and forth. This is usually described as the struggle between impulse and defense. In perceptual terms, the impulse and defense could be considered as one ambiguous temporospatial Gestalt, accessible to consciousness ("You're looking right at it; why can't you see it?") and perceived in one way or the other (s) according to the psychological attitudes or set of the moment.

Though we have evidence of the existence of a primary, transitive, more or less Gestalt-free mode of perceptual organiza-

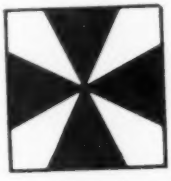

Figure 5

tion,‡ it tends to be very quickly organized into Gestalt configurations. At least a portion of this process of organization is described in psychoanalysis as secondary revision. Images which are especially influenced by unconscious processes indicate this by their ambiguity, and hence their relationship to a more primitive mode of mental organization. Kris[19] suggests a generalization: "Configurations which bear the imprint of the primary process tend to be ambiguous, allowing for more than one interpretation." Schilder[26] points out:

> Once repression has taken place, the image that appears no longer has the self-certainty and self-containedness of those images that are not built on repression. Moreover, it must be asserted that the repressed is in some form present in any image that represents it. To decide in what form it is present is an important issue. These formal considerations have a limitation. The conception of a sharply circumscribed image is but a theoretically postulated limiting case; it will never exist in reality, because every image and every percept is the consummation of drive attitudes; and in the final analysis, my prior attitudes enter every perception and memory of mine, without my being fully conscious of them. In this sense every image has a "symbolic" overtone. There are always pre-phases in which condensations have taken place, and since nothing psychological is ever lost, the image is surrounded with this pre-history as a halo.

I have noticed that drawings with notable ambiguity are not produced after very superficial contact with the patient. They appear after a little deeper relationship has been established, and the repressed is thereby encouraged to emerge. The three drawings (Figs. 1, 2, and 3) were made by patients who had been interviewed a number of times and with whom a therapeutic relationship had been established. Ambiguity of this sort was rarely observed in drawings of subjects seen only once and for testing purposes.

Configurations bearing the imprint of the repressed are unstable, and on scanning, or the application of attention, tend to break down, and other configurations then emerge. When a new configuration emerges, it becomes figure, and what was previously figure becomes field. An idea or image is for the moment the only possible image, and that which had been there previously can be recalled only by alternating with the original percept, as in the example of the cross (Fig. 5). Ruesch discusses it as follows[24]:

> Complementarity, which means this: that the human being at any one moment can look at only one thing. At Time One, he can study Phenomenon A; at Time Two, he can study Phenomenon B; and at Time Three he can study Phenomenon C; but never can he study them all at any one moment. Basically, we focus upon one thing, and we neglect other views for the sake of obtaining better views at that moment. . . . In human communication we usually are not able to say what the things are on which we do not focus; but we are at least vaguely aware of the existence of the neglected aspects.

This is what Kris described as disjunctive ambiguity, "when the separate meanings function in the process of interpretation as alternatives, excluding and inhibiting each other."

Set; Directive State

It is well known that the observer's set or attitude will influence perception. Observers instructed to see a figure in one way will tend to see it thus, though it may be ambiguous and capable of being perceived in another way. Frenkl-Brunswik[5] showed how emotional rigidity interfered with perception of ambiguity in prejudiced persons. Schafer and Murphy[25] have presented evidence that reward and punishment influence the perception of ambiguous figures.§

The influence of bodily needs, for example, hunger, of reward and punishment, values, personality; the effect on perception of emotionally disturbing stimuli, have been

‡ This distinction corresponds to Werner's[27] differentiation of syncretic and discrete organization. Ehrenzweig[3] discerns, behind the level of organized configurations, a fluid area of perception dominated by the primary process. He describes how, by such techniques as long fixation (prolonged staring), objects lose their thing quality, and undergo various distortions.

§ Köhler[18] states: "From the viewpoint of Gestalt psychology, a change of attitudes involves a definite physiological stress exerted upon a sensory field by processes originating in other parts of the nervous system and to some degree the organization of the field may yield to it."

the subject matter of many experimental studies of perception in the past 10 years. The motivational-functional elements in perception have been contrasted by Bruner and Postman with structural-formal elements of perception. There is considerable experimental evidence that the motivational state, need, or set of a subject influences his perception. The ambiguous figures presented to consciousness (PCPT-CS) by the preconscious are thus perceived in accordance with a need state of the perceiver. This facilitates repression by means of the selective effect it has on perception. Murphy [22] believes that "the perceptual field comes to take on a structure in which the acceptable, the good, the satisfying, tend to take the dominant position."

The concept of set was originally related to muscle phenomena. The subject was set for a particular task by a state of muscular tonus. This is exemplified by a patient with strong resistances who, by dint of intensive analytic work, became aware of a realm of inner feeling whose exposure he had been stoutly opposing. At this point he felt like "firming up," to which, when asked, he associated bristling like an animal which is threatened. The firming-up represents a restoration of a chronic defensive process of withdrawal into a smaller perimeter. This tension is in effect a set which enables only one sort of perception to prevail.

Attention Span; Immediate Memory Capacity

Another limiting and complementary factor in repression is the attention span of the individual subject. This involves the number of discriminations that can be simultaneously made by consciousness and how many acts of attentive cognition can occur simultaneously. Woodworth [28] cites experiments whose conclusion is "that simultaneous performance of two attentive acts of cognition did not often, if ever, occur." ‖

Miller [21] presents interesting ideas concerning the limitations of our capacities for absolute judgments. Along a unidimensional scale in various sensory modalities this capacity seems to be about 7 ± 2 judgments. Especially interesting for psychoanalysis is the question of immediate memory for "chunks" of information, which also seems to be about 7, but which may be increased by recoding so that the seven chunks of information may contain many more "bits" of information. As an example of recoding, Miller mentions the learning of telegraphy. First, individual "dits" and "dahs" must be attended to, then words, then phrases. An immediate memory for seven different "dits" and "dahs" becomes an immediate memory for seven words or phrases—larger chunks, containing a number of bits. This process of an apparently innate limitation in the capacity of immediate memory, and the way in which it is gotten around by recoding, is another aspect of the process of condensation which enters into the formation of the ambiguous figures and images of our mental experience. The extent of condensation or recoding is shown in the manifest content of our most famous dream—of Irma's Injection. The text of the dream occupies ¾ page; the associations, admittedly incomplete, occupy 10 pages. And to understand the dream, recoding must occur; that is, an interpretation condensing the meanings of the various associations must be made. Miller says [21]:

> Our language is tremendously useful for repackaging material into a few chunks rich in information. I suspect that imagery is a form of re-coding, too, but images seem much harder to get at operationally than the more symbolic kind of re-coding.

The limitation in capacity of immediate memory, as well as the limitation in attention span of the individual, may be considered to be ego characteristics or apparatuses. These two limiting factors combine to facilitate repression. In both, the life ex-

‖ The aim of cubist paintings, to represent simultaneously more than one view of an object, might be considered as an attempt to represent several acts of cognition or perception simultaneously or as a kind of synthetic reversal of condensation. As we know, this may cause certain difficulties for the viewers.

periences, personality, and current attitudes of the individual, influence, for example, which particular aspect of a percept shall occupy the center of consciousness at a given time, and, so to speak, which "bits" in the chunks of information available shall be picked out for attention by consciousness. By the occupation of consciousness by one image or percept, others are excluded.

There is reason to think that perception occurs in brief flickers. Thus, Hebb[11] states:

> If the duration of an idea, or a perception, is the duration of reverberatory activity in a closed system, one can say that the pattern of activity rarely lasts without change for as long as a second. The stability of a perception is not in a single persistent pattern of cerebral activity, but in the tendency of the phases of an irregular cycle to recur at short intervals.

If perception is thus a series of tachistoscopic presentations to consciousness, so to speak, prevailing attitudes or set, reinforced by limitations in attention span and capacity for immediate memory, effectively influence which flickers or frames are attended to and which are not registered.

Comment

Many dreams, images, and ideas are presented to consciousness in an ambiguous way. If they are represented in a drawing, the drawing has the characteristics of an ambiguous figure. This characteristic of ambiguity is a consequence of several factors. These include the process of condensation, described by Freud as due to the mobile cathexes of the primary process. Condensation also occurs to avoid the censorship, and it also exists as a consequence of the limited attention span or capacity of immediate consciousness and the limitation of immediate memory. This limitation in capacity serves repression by making it possible for consciousness to be occupied or occluded by percepts, ideas, or images which are acceptable to consciousness, at the same time excluding unacceptable mental elements.

Images are presented to consciousness as more or less organized temporospatial Gestalten. This is because of the tendency of the mind to perceive in configurations, an important tendency manifesting itself in secondary revision. The tendency to patterning is so great that even when few cues actually exist, organization and form are superimposed on the stimulus aggregate.

Gazing at, scanning, considering, or associating to these images causes a breakdown in their surface Gestalt structure, and competing (repressed) structures can then come to the fore. This emergence of repressed structures may occur as a figure-ground reversal or as a result of changes in role or identity of the original figures. One of the important ways by which ambiguous figures are produced is through the superimposition of various memories and images, which the unconscious ego attempts, with varying success, to fuse into a realistic unit or configuration. These images may be regarded as tied together by laws of association, but they could also be considered as held together by the force of a field. That repressed ideas and feelings attach derivatives to themselves is essentially a field concept. The field is organized by the energy of the repressed, the derivatives occupying different loci in it.

The notion of superimposition is implied in such ideas as "levels" of awareness, conflicts, fixations, etc. We say a particular psychological phenomenon means this at a superficial level, that at a deeper level, and at the deepest level of all, something else. What does this mean? Partly it is a reference to the development of the particular phenomenon in whose formation different eras and events of life participate. But it is also a reference to the fact that a number of different memories and percepts combine to form the given structure, and this combination is in the nature of a superimposition. The diagram of the memory system in Chapter VII of "The Interpretation of Dreams" is an example of this concept.

The analysis of dreams by association to each individual element in the dream, as described by Freud, may be considered a

technique for scanning this composite to discern the elements that make it up. One might say that the work of association has occurred in producing the image and that the work of analysis consists of scanning it. The question: What do you associate to this? or What does this bring to mind? could be asked in another way, as: How else could you look at this? or How else do you perceive it?

The ideas presented in this paper bear on a number of common clinical observations in psychoanalysis. One is that change in psychic processes is not simply a quantitative linear function. Rather, leaps and jumps do occur. For example, in insight something is not known, and then (as in the ambiguous figures) it is suddenly known or seen in a different way, and there is no intervening step. A total reorganization of the field has occurred apparently instantaneously and in a quantal fashion. This is true also of alternation in feelings, such as are found in ambivalence, where one sometimes sees sudden and startling reversals, as if an end-point of one type of reaction has been reached and then there is a leap into the opposite. When the leap has occurred, the idea or feeling which previously existed is at least momentarily excluded from consciousness.¶

Associated with fresh insight, the feeling is often described: "I knew it all along." The repressed is then not alien but was there buried in the figure or forming the field.

The viewpoint presented here is largely due to emphasizing the spatial, pictorial, configurational qualities of those temporospatial Gestalten which we term dreams, images, ideas, and feelings. This is in contrast to our customary temporal associational emphasis, influenced by our reliance on the stream of speech.

¶ Werner[27] quotes from Lecomte Du Nouy's book, "Biological Time." "All our experience leads to the admission that continuity exists nowhere, and that one of the roles of consciousness is to manufacture continuity from discontinuity."

Summary and Conclusions

1. A drawing of a dream or image often turns out to be an ambiguous figure. That is, when its creator looks at such a drawing, it may suddenly take on a new meaning, or a previously unrecognized aspect may become apparent, frequently of opposite significance to the original conscious intention of the drawing.

2. This ambiguity is the result of condensation. Two or more images are combined into one, often by means of superimposition, in order to produce a unified, "reasonable" picture for consciousness.

3. As we are able to keep only one idea or image in the center of consciousness at one time, awareness of and concentration on one (manifest) aspect of an ambiguous figure successfully keeps the latent (objectionable) meaning from becoming conscious. If we did not have this innate limitation in span of immediate consciousness, we could be simultaneously aware of more than one aspect of an ambiguous figure.

4. By looking at, scanning, the ambiguous drawing of a dream or image, the buried meaning often becomes apparent. The technique of dream interpretation, in which each element is associated to, may be considered a way of scanning an image to look for its latent meanings.

5. The function of repression is in part dependent on the fact that condensation presents consciousness with ambiguous figures whose buried meaning is unrecognized because the emotionally determined set or attitude of the subject causes him to see only one aspect of the ambiguous image, and this concentration on one aspect of the image is further helped by the fact that it is possible to be immediately conscious of only one idea or image at a time.

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The Organization Factor as an Explanatory Principle in Functional Psychosis

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Introduction

In a recent paper it was suggested that treatment methods in psychiatry produce alterations in the phenomenological field or in the organization factor.[1] This paper will describe the role of the organization factor in the development of functional psychosis.

Some Clinical Considerations

In individual psychotherapy the remarks made by the therapist are intended to communicate to the patient information that will maintain the therapeutic process, whether the remarks are in the nature of interpretation, confrontation, or reassurance, or are evidence that the therapist is listening or simply that he is present. His gestures, if he is visible to the patient, are similarly intended. With patients who function principally in secondary process, the end of communication is usually best served when the behavior of the therapist is appropriate to, or on the same level of discourse as, or in the same frame of reference as, that of the patient. Usually it is not conversational, not colloquial, or even in poor taste, to make a "wild," "deep," or "direct" interpretation. Eventually there must come, as it does to all men and bulls, a "moment of truth," when the therapist must plunge through the tissues, leaving a draining or a bleeding sinus. If he goes wide of the mark, he may or may not get a further chance at deep interpretation.

When patients produce principally in the primary process, their perceptions are probably in terms of the primary process content, meaning, or significance of the therapist's words or gestures. This is probably true whether or not the therapist intends his communication to be in primary process. In any event, one is not usually as colloquial, idiomatic, or reality-oriented with the psychotic as he is with the neurotic patient.

In group psychotherapy the situation is again different, for the patients' productions are varied, not only in that they consist of different proportions of primary and secondary process, especially in heterogeneous groups, but also in that the behavior and complaints of the patients are symptomatic of a more or less wide variety of diagnostic categories and psychodynamic mechanisms.[2]

For example, in a recent session, an all-male group was telling me its collective reasons for hospitalization. The first patient to my left advised that there was nothing wrong with him, but that he was there because of the workings of the mental health movement. A second patient said that he was having trouble with his wife. A third said that his trouble was because of his sister, who feels that she is "a little queen." Another patient said that he was frightened because of what voices were saying to him. Another patient said that he had been depressed, while still another said that he used to hear noises in his head.

Since the patients were all talking about the same thing, each in his own way, it was evident at this point that there was a high degree of organization in the group. According to my procedure, this was the time for a binding, interpretive comment from the therapist.[3] The forthcoming interpretation was to the effect that everyone in the group had become the way he was for a reason, and that, even though their troubles

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seemed to be different, their underlying problem was the same, namely, the inability to express the appropriate feeling—in this case, hostility—to the appropriate person at the appropriate time.

At the moment it is not my purpose to consider whether or not this was the proper thing to say or whether this was the proper time to say it, or even whether or not the concept itself is correct, namely, that the patients' various mental states did actually result from strong feelings of resentment toward significant figures in their early environment.

Therapeutically, at least, the formulation appeared to be worth while, for treatment was maintained, with the patients inquiring specifically how they had reached their present state.

My explanation for this was that they had not liked what was happening around them, that it had been too painful to them, and that they had started paying attention to other things that were available to their consciousness, i. e., other things in the phenomenological field. In brief, they had been hiding out to a greater or less degree, and had been practicing this technique for many years.

For the sake of completeness, it should be added that this interpretation was made at a time when strong transferences existed; of the six patients in the group, three had strong paternal and three had strong maternal transferences to me. The three patients who saw me as a strong father were discharged within the next two weeks; those who saw in me an understanding mother are still hospitalized. With the aid of a nurse, we are working through their feelings of resentment. The disorders of these latter three patients are earlier and deeper, and take longer to resolve.

Clinically, I would say that my interpretation (to be considered not as purely a single event but as a line of treatment) had value in restructuring the phenomenological field for all six patients. Three of them apparently perceived and responded positively to my advice to stop hiding and to get out into the world and make a go of things. The other three may have gotten my message, but their response was either to let it pass or to burrow in deeper, knowing that I did not really mean to send them out into the cold. Whether or not changes were produced in the organization factor will be touched on later in this paper.

Some Theoretical Considerations

Ideally, of course, the principles on which treatment are based should be isomorphic with etiology. Treatment should stem from cause. This, obviously, is not always the case in psychiatry, although I should consider certain environmental manipulations—when clearly based on patient needs rather than on expediency—and deep psychotherapy to be etiology-based.

It is possible, however, that treatment may be right for the wrong reasons. To go further, it is possible for a theory of treatment to be "correct," on a certain level of analysis, while the principles on which it is based may not account for the existence of the illness in the first place.

I do not consider this to be the case with the general theory of treatment which I recently proposed. Specifically, to concentrate for clarity on a single, though important, example, I consider the signs and symptoms classed as schizophrenia to have as their basic psychopathology, to have developed with, and to be isomorphic with, a dysfunction of the organization factor; the signs and symptoms are manifestations of organization factor dysfunction.

Etiological treatment, then, would have to be directed toward eliminating the dysfunction in the organization factor. Before we can consider how this is to be done, we must first consider how the dysfunction originates.

In the original word-sorting experiment, from which the organization factor was derived, its role was to mediate between performance and explanation of performance; i. e., for the stimulus question "What

have you done?" to be answered appropriately, the subject had to refer back to his actual performance on the Word Sorting Test.[4,5] This required some sort of memory trace or engram to have been established, capable of being recalled to the level of awareness on which the question "What have you done?" was perceived. Eventually, from the available store of verbal responses, one had to be selected which would describe the subject's recalled behavior not only to his own satisfaction but also to that of the experimenter. A result of this experiment was to demonstrate that the dysfunction in the behavior of schizophrenics lay not in their ability to sort, for they were able to do this as well as normals of comparable educational achievement, but, rather, in the eccentricity or lack of communality in their answer to the question. The difficulty was not in their ability to perform, not in their ability to verbalize, but in their ability to relate verbalization to behavior in the same way that "normals" did. It was formally stated that the defect was in the organization factor.

But what accounts for the defect in the organization factor?

The Principle of Functionalism

One observes among physicists no reluctance to forsake the notion of "hardness" in matter. Yet among physicians, perhaps because medical training begins with a dead body on a cold and hard dissecting table, and perhaps for other reasons, the basic faith is that somewhere in the human anatomy lies the explanation for human behavior. This point of view is characterized by the statement: "Structure determines function."

The weakest word in the preceding statement is "determines." A statement more satisfying to my taste would be: "At any given moment, the structure of a bodily part limits its function." I cannot grasp an object by the dorsum of my hand, nor can I scratch my right ear with my left ear. However, the reverse fact, that an act is physically possible, has only limited predictive power for the occurrence of that act.

The usual argument to be introduced at this point is to the effect that if we had the most complete microdescription of structure, we would *know* whether or not an act would occur. Without laboring through the steps of this argument, we may short-cut to its final statement: "If all the information from one computer (here being the brain and nervous system) were fed into another, equivalent, computer, the second would reach the same answer as the first." With this we can all agree. However, we may not all accept the computer-model of human behavior, finding it of limited usefulness.

Structuralism exists in forms other than the narrowly anatomical. It is logical here to include physicochemical, and certain of the physiological, approaches. When "mind" starts to enter the picture, as in psychophysiology and in psychology, it is time to consider the concept of functionalism.

I scarcely feel able to argue the cause as well as William James,[6] nor do I believe that our understanding has progressed significantly since his time. Historically, the position of functionalism developed out of and in reaction to the structural psychology of the 19th century, which has nevertheless persisted into the 20th. It is principally the ontologic aspects of functionalism to which I should like to make reference at this point, although perhaps not in the language of William James.

Let us grant first the *Anlage* of the fertilized ovum, and then the influences of the prenatal maternal environment; nor is this cursory acknowledgment intended to minimize their importance.[7] The neonate may again be considered as an *Anlage*, but with different, though overlapping, parameters describing its potential for modifiability.[8] In the process of development of

organs into functional systems,* and as functional systems "learn" to perform psychological acts,† the *Anlagen* are caused to develop in a particular direction. This development is *somatic;* the actual body tissues grow in a certain way as a result of reinforcement of functional behavioral or microbehavioral patterns. Reinforcement here is specifically thought of in analogy with the terms of Hull [10] for "elicited" acts and of Skinner [11] for "emitted" acts, although Skinner's early "empty organism" formulation led him to consider a class of behavior exclusively in terms of bar pressing, with no regard for somatic processes temporally preceding this effect; in the present context this is too strictly operational a view.

As the organism matures, the different parameters of modifiability become altered in relative magnitude, some parameters of growth dropping out, later to be replaced by decay functions. This is generally spoken of as decreased modifiability, or as increased rigidity, but it is actually the potential for modifiability that has been decreased, as apparent rigidity may be produced through dysfunction of the organization factor.

The organization factor is a functional system that is dependent on the existence of certain neural mechanisms which have not yet developed in normal childhood but which persist into old age, even when attended by cerebral arteriosclerosis. The organization factor is, however, nonfunctioning in advanced dementia paralytica (general paresis). It functions in schizophrenia, but in a way that is unusual, in the statistical sense.[4] At any given time it must rely on certain neural tissue or mechanisms, but what the underlying neural tissue or mechanisms are is unknown at this time; it is, however, evident that they are "central" rather than "peripheral." Like "underlying neural mechanisms" in general, this one may be poisoned by chemicals, but it is even more remarkable how the entire mechanism of attention may be altered by sensory restriction, while the most striking and immediate changes in this function may be accomplished by the relatively simple procedures of suggestion and hypnosis.

The argument is invariably presented that any functional mechanism which may in some measure be influenced by physicochemical means is ultimately reducible to physics and chemistry, and that pathology of this mechanism will ultimately be best controlled by physicochemical means. Such an argument is rarely offset by the information that at the moment physicochemical techniques are relatively feeble in this regard, while suggestion, hypnosis, milieu effects, etc., are quite potent. The reductionist position, of course, denies the present facts of medical psychology. More serious from the reductionist viewpoint is its own failure to apply the parity principle of time invariance to its understanding of functional mechanisms. Learning is carried on in conventional forward-moving time; functional tissue growth progresses in such a way that the functional state of any tissue at time $t_1 + m_1$ minutes depends on the tissue state at time t_1, and on the learning experience between t_1 and $t_1 + m_1$. The functional state at $t_1 + m_2$ depends on the learning that went on between m_1 and m_2 as it was learned by the organism at $t_1 + m_1$—*not* by the organism at t_1 or at any other time. It is hard to visualize a physicochemical means whereby time would be made to reverse itself, so that an organism could be made to "unlive" its life and ungrow its tissues and functional mechanisms in a manner compatible with "good

* A functional system implies not merely the groupings used in textbooks of medicine, such as cardiovascular or cardiorespiratory, but complex groupings which cut across these systems, as, for example, the functional system involved in producing bronchial asthma, involving somatic and autonomic nervous systems, striped and smooth muscles, the respiratory apparatus, a system of memories, a redintegrative mechanism, a "trigger" percept serving as the redintegrative stimulus within the phenomenological field, etc.

† A psychological act may perhaps best be defined by contrast with Sherrington's statement: "The pure reflex is a school at which the 'I' never was"[9]; a psychological act is a school at which the "I," however primitive, certainly was.

mental health." However, I am willing to grant the possibility that time invariance may not hold for functional systems; I do not believe this to be the case, but I cannot deny the possibility.

Growth of the Organization Factor

The organization factor has now been described as a functional system, and has been singled out as that particular functional system which accounts for functional psychosis.

It follows that functional psychosis is not a "disease," but, rather, is a way of behaving of organisms that have had a particular kind of life experience. This experience has produced a functional mechanism with characteristic modes of response to certain life experiences. The mode of response is characterized by selective attention to certain parts or aspects of the phenomenological field, similar to that occurring under conditions of sensory restriction or under hypnosis.[12]

It becomes a matter of great theoretical and practical importance to learn the time schedule along which the organization factor develops. The "concrete" and "pseudoconceptual" thinking of the child and young adolescent [13] indicates an inability to relate parts of the phenomenological field in an "abstract," or "conceptual," manner, suggesting incomplete development of the organization factor. This is significant, since that which is as yet incompletely developed may yet be molded.

It is well known, of course, that the average normal adult does not function customarily on the highest conceptual level, but that he thinks, rather, in "complexes," in little bundles of more or less complete, more or less closely associated ideas. The Vigotsky Test [14] and my own Word Sorting Test prove difficult even for college-trained adults. The average normal adult, however, can be made to see abstract relationships even when he does not spontaneously arrive at them himself [4,13]; it will be of interest to find out to what extent abstracting ability can be trained, for this will bear on the modifiability of the organization factor in the adult. This is quite important in view of the proposition that a well-functioning organization factor can produce workable structure in a disorganized phenomenological field.

What kind of life experiences affect the development of the organization factor? While no specific answer can yet be offered, I believe that we know a good deal about what constitute healthy, formative childhood experiences. I have no new information to add to that currently available in the literature and in individual clinical experiences. Obviously, a childhood and early adolescence which enhances breadth of experience with the possibility and the encouragement to formulate a wide variety of interrelationships in the affective, cognitive, and conative spheres might be expected to aid in the development of the organization factor. On the contrary, a life which tends to limit experiences, which encourages narrowness of perception and rigidity of response, would be expected to limit development of the organization factor.

These few remarks may serve as a beginning frame of reference from which to view the concept of schizophrenogenicity in a manner compatible with functional psychology, the experimental work on sensory restriction,[15] and recent developments in ego psychology.[16]

Implications for Therapy

There is much to be expected from the psychosocial approach to schizophrenia; the organization factor apparently continues to develop well into the teens, and the average adult appears to utilize this function in a very limited way. Accordingly, there is remarkable opportunity for development, probably throughout life.

Since so much of research in schizophrenia is currently directed toward biological factors, some attention should here be paid to what this may be expected to yield.

From the viewpoint of organization theory, probably the most significant area for biological research is genetics. Embryology appears to have proved a point: At least during the prenatal stages of development, the genetic endowment of the organism appears to be the prepotent determinant of growth. The present theory, of course, depends on the proposition that this does not hold true after birth. Since the limits of basic structure lie in the genes, the importance of research in this area cannot be overestimated.[7]

Genetics, however, affords the present generation none of its desirable consequences. Accordingly, through biology, chemistry, and physics, ways have been sought to interfere with the somatic mechanisms required to sustain the life of a psychotic or neurotic patient, in hopes that his undesired behavior will be eliminated, and not too much else added or subtracted.

As indicated earlier, owing to time invariance, an elegant solution can scarcely be expected on this level. A dynamic growth process cannot be reversed in time. Indeed, a Nobel prize in physics has been awarded Yang[17] and Lee[18] for demonstrating loss of parity under what are generally accepted as the conditions for left-right, or mirror-image, symmetry. What would it mean for conservation of parity if time itself were reversed, or "mirror-imaged"? Yet to reverse time is precisely what we do not know how to do, despite the demands of logic.[19]

Failing an elegant solution, a practical one may yet be sought. One can imagine a "clean" drug, with minimal untoward side-effects, that would knock out the sensorimotor patterns of psychotic behavior, yet leaving the patient trainable along socially acceptable paths. Of course, such patients would display a characteristic "as if" quality to their behavior that would leave them readily identifiable as schizophrenic.[20] To comment again on the inelegance of such a solution would be redundant.

All paths seem to lead again to the broad psychosocial area, with identification of the patient as a psychosocial unit. He has, to be sure, a genetic endowment determining the absolute limits of function, but his behavior will not be predictable from these parameters. Behavioral science seeks to establish the relevant laws; it must be encouraged to develop, mindful of, but not restricted by, the facts of structural existence.

Summary

The organization factor is described as a functional mechanism, and its etiological relationship with functional psychosis is described, with particular regard to schizophrenia. Development of the organization factor is presented in biological and in psychosocial terms, and the logical limits of modifiability by various means are demarcated.

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Explorations in Psychotherapy

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The singularly pervasive effectiveness of lysergic acid in altering the subjective experience and objective behavior of those to whom it is given affords unique opportunity for exploring methods of psychotherapy. Two attributes of lysergic acid psychoses especially favor such study. First, there is no impairment of consciousness during the psychotic reactions. Second, the severity and duration of the reactions and their relation to dosage have been well established. The researcher in psychotherapy has the opportunity to observe the psychotic reaction from its inception to its termination and the advantage of having a subject with whom he can communicate during the entire experience. He thus occupies a position which allows him to judge both the immediate and the enduring effects of any psychotherapeutic methods he chooses to use, and which frees him to employ a series of methods on a trial-and-error basis.

Before proceeding with the method of psychotherapy which is the subject of this paper, it is necessary to give an account of certain facts which characterized this study of the effects of lysergic acid on human subjects. In particular, certain subjects volunteered (for a variety of reasons) to take lysergic acid with the knowledge that it has a reputation for producing mental and emotional changes which last about 8 to 12 hours. In taking the drug, they understood that they had entered a contractual relationship in which they had agreed to give investigators information about themselves as experimental subjects. The agreement was nonpersonal and had nothing to do with individual worth or uniqueness. The personal factors which underlay the subject's motivation in volunteering to take the drug were not fully known to the subject himself or to the researchers. Personal and personality factors which underlay interactions between subjects and researchers were also only partly known. Within this context of unknowns were a number of known factors; namely (*a*) the declared willingness of the subject to take the drug and to be examined and experimented upon, (*b*) the dose and chemical structure of the drug, (*c*) the express motivation of observers to give their attention to the subject and to record his words and actions, (*d*) the express motivation, method, and procedure of psychologists, psychiatrists, and physiologists in their examination and experimentation upon the subject, and (*e*) the general plan of the experimental day and the sequence of structured and unstructured blocks of time.

In short, the experimental day was the most inclusive unit with which the research dealt. It represented a drama in which the subject, observers, researchers, patients, and chance subjects were the actors—a drama in which some of the acts and scenes had been rehearsed and prearranged, and in which others were left to the subject's participation in the chance events.

For the subject, the experimental day was a period of time during which he had a variety of experiences arising both from physiological changes in his tissues and from an ever-changing social matrix. He began the day with a more or less well-defined somatopsychic state, altered in some degree by the cues he perceived from those

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who accompanied him and administered to him the drug. From this moment forward, he was distinguished from everyone else both in his own mind and in the minds of those about him as *the subject*. Within about an hour's time, cutaneovascular changes took place which he felt, and which others observed, as blushing, pallor, and perspiration. These changes were soon accompanied by neuromuscular changes, which he felt as heaviness, lethargy, and weakness. These events marked the subject irrevocably and undeniably as different from those about him. Psychological changes also made their appearance during the first hour and increased in magnitude during the following two hours. The subject became confused and anxious; his visual perception of external objects became distorted, as did his general sensory perception of his own body. He was pervaded by an undefinable sense of unreality and by a more definable experience which he could express in words having the connotation of "awareness." He was generally distressed by the over-all unpleasantness of his experiences; yet he became more gregarious and, to a less degree, more hostile with others.

Review of the research records from a purely subject-centered point of view sorely tempted the research workers to evaluate the above phenomena as entirely physiological and endopsychic in origin and as directly attributable to the specific action of lysergic acid, as ringing in the ears is to large doses of acetylsalicylic acid. The nature of the subject's interactions with others was, from this point of view, considered wholly secondary to the specific action of lysergic acid. Such an interpretation, it turned out, became untenable when data about the subject's interpersonal relations were studied from the larger perspective of social psychology. Indeed, when all the available facts were assembled, scarcely any specific psychological effects of lysergic acid could be identified which could not better be accounted for in terms of social factors identified by the research observers. In other words, the personal meaning or significance which the subject attached to his total situation was based fundamentally on reality.

The experimental situation, by its very nature, confronted him with the conflict-provoking problem of a contradiction, for it freed him in large measure from responsibility for his acts but, at the same time, demanded that he reveal the personal and intimate thoughts behind them. He had full license on the condition of full confession. The less he did, the less he had to confess or explain. Yet deliberately doing very little or acting very proper was not fulfilling the obligation or expectation to participate cooperatively in the research endeavor. He was constantly confronted with doubt as to whether his words and actions made public would be interpreted as products of his private self or merely as drug-induced aberrations. He might also have been harassed by pernicious doubt that he had received the drug at all, if he thought of the possibility that he had been chosen as a control subject. He could then contemplate suffering the indignity of being a dupe to his own guilty conscience and of knowing that he was in the position of being "damned if I do and damned if I don't."

A word of comment is necessary to enlighten the reader as to the circumstances which led the research team to regard phychotherapy as a feasible undertaking in a chemical psychosis. The similarity between lysergic acid psychosis and schizophrenia was sufficient to suggest that psychotherapeutic methods developed for treatment of the latter might be of value in the former. More important, however, than the purely theoretical consideration was the circumstance that the research design included continuous observation of every subject throughout the experimental day and a sociological analysis of his interactions with other people during that period. The results of this part of the research demonstrated clearly that the se-

verity of the subject's reaction to lysergic acid and the intensity of his symptoms were extremely variable and fluctuated in accordance with the nature of the subject's social situation and the personalities of the other subjects in it. By actual count, 16 out of 23 subjects experienced alteration of symptoms as a result of fortuitous interaction with others. It was impossible, in effect, to designate in advance which situations would be a "therapeutic situation" and which would be a "pathogenic situation." In addition to these fortuitous interactions was the unplanned circumstance that some of the subjects made direct appeals to the available psychiatrists for help during the most trying period of their reaction to lysergic acid. The occurrence in several instances of rapid and dramatic disappearance of symptoms during ensuing therapeutic interviews was further basis for the conclusion that the research project should include a psychotherapist who would attempt psychotherapy of the subjects on a scheduled basis, rather than leaving it to chance.

Five of the psychiatrists and one sociologist associated with the lysergic acid research project served as psychotherapists to one or more of the subjects. Their collective experience as psychotherapists in this situation is the topic of this paper. Data on six of the subjects are incomplete and hence are not reported here. Three of these were given therapy by psychiatrists and three by a sociologist. The experience of the five psychiatrists with 15 other subjects is reported here.

Psychiatrist J. D. has had 20 years of experience in the hospital care of psychotic patients, has undergone personal psychoanalysis, and has his private practice in which he does psychotherapy. He had taken lysergic acid to learn its effect on himself. His role in the research project was that of interviewing subjects for the purpose of diagnosing their reaction to lysergic acid. In the course of one such diagnostic interview, the subject unexpectedly put him in the role of a therapist. He felt considerable sympathy for the subject and responded to her spontaneously.

Subject 1, a single woman, a college student, aged 19, was a patient in the hospital with the diagnosis of acute undifferentiated schizophrenic reaction. While interviewing this subject, the psychiatrist gave up his goal of making a diagnosis and interceded in a friendly way to spare the subject further distress. His intercession took the form of forceful insistence that her excessive pace of speech and her hyperactivity were a way of escape from thinking about the disturbing preoccupations which had played an important role in leading to her admission to the hospital. He also told her of the strange unreality he himself experienced when he was a subject of a lysergic acid experiment. This was followed by a dramatic change in her behavior, and the expression on the subject's part that she suddenly realized that this was not a prearranged play, and that people were not influencing her thoughts.

Subject 2, a 20-year-old college student, male, another subject interviewed by psychiatrist J. D. for diagnostic purposes, also showed considerable distress, to which the psychiatrist responded by assuming the role of therapist. He exhibited anxiety and feelings of guilt which were related in part to erotic feelings and preoccupations about old sexual experiences not hitherto revealed to anyone. After catharsis of these preoccupations, the anxiety and guilt markedly diminished.

With this subject, the psychiatrist's matter-of-fact approach in interviewing for diagnostic purposes was regarded as a secure situation which permitted him to speak freely about a homosexual situation which had occurred years before, but which had tormented his thoughts ever since. The psychiatrist's matter-of-fact discussion of this subject material greatly allayed the subject's anxiety. Indeed, by his own report at a later date, he said he had felt better since the interview than he had *before* the lysergic acid experiment.

Psychiatrist R. W. H., with seven years' experience in psychiatric research, in care of psychotic patients, and in psychotherapy of character disorders, was director of the lysergic acid project and had taken lysergic acid himself to learn its effects. He was available to subjects throughout the experimental day, and he was sought out by Subject 3, married, aged 28, a registered nurse, and head nurse on the disturbed ward. At the peak of her lysergic reaction, this patient became painfully depressed and lonely to a desperate degree. It was while in this state that she sought out R. W. H., as director of the research project, with the hope that he could help her. He accompanied her to lunch, with two observers, at a restaurant near

the hospital. In this informal setting, he responded to her in a good-humored, chiding way. He informed her that he saw her as more concerned with her duties as a nurse in her lysergized state than he himself and others are in their normal state. Her mood rapidly changed from depression to lighthearted playfulness and a great increase in spontaneity in interaction with everyone she met. Later in the day her mood became depressive, but not to the degree it had been.

Subject 4, real estate salesman, aged 24, sought psychiatrist R. W. H. to accompany him to lunch outside the hospital. While at the restaurant, he brought out his fears of homosexuality and his problem in becoming less dependent on his mother. From the subject's point of view, it was possible to discuss these matters because the psychiatrist communicated complete acceptance of him and indicated that he had similar fears and problems himself. The subject was most impressed that he could let himself be his "real self" and still be accepted as a legitimate subject of discussion, worth understanding. Several days after the experiment he reported this discussion as being of great positive value to him.

The third patient with whom psychiatrist R. W. H. played the role of psychotherapist was Subject 5, a nurse, aged 23, a married woman.

She sought out psychiatrist R. W. H. when she began feeling anxious and disturbed over her perplexed thoughts and unreal body sensations. Her presenting complaint on coming into his presence was that she felt "so queer" but could not understand what she felt queer about or even what the queerness was. She responded to the psychiatrist's encouragement to talk out her experience but still felt very uneasy about her queer feelings. The psychiatrist then changed his approach by seeking to provide her with a concept of how she felt and finally struck on the idea of nonexistence. The idea of nonexistence had an unexpected appeal, which not only allayed the subject's anxiety but also led to the realization that nonexistence was attractive because it would solve a difficult problem in her life. The extent to which the experience was significant to the subject is indicated by the fact that a few days after being a subject she made and acted on a decision which greatly altered her life.

Subject 6 was a single man, a medical student, aged 24. During the severest period of his reaction he underwent a cross examination by four members of the research team. With the pressure of time, the demands put on the subject to satisfy the investigative function of the researchers became progressively severe. At the same time, the experience reported by the subject became more and more devastating until he was finally possessed by the delusion that he was a walnut, the meat of which was his brain. His delusion progressed a step further, to the point that the meat of his walnut-self floated off into space and disappeared. While relating this delusional experience, the subject complained of his energies being drained out into the room in which he was sitting. Finally sensing the real nature of the complaint, psychiatrist R. W. H. responded to it as an expression by the subject of his feelings with respect to being questioned in an impersonal way, as though he were nothing more than a living guinea pig. The other researchers recognized the point of this interpretation and immediately apologized to the subject and told how they resented being asked questions that were purely for the scientific record. With this change in the discourse between the researchers and the subject, the latter visibly brightened and then good-humoredly reported the sensation that energy was flowing back into his walnut-self. Finally, he reported that the "walnut feeling" had gone, that he had arms and legs again, and that he felt like himself. He also ceased reporting delusional material.

Psychiatrist J. S. B. (author of this paper), with six years' experience in the care of psychotic patients and in psychiatric research, was engaged by the lysergic acid project for the express purpose of exploring the feasibility of psychotherapy in lysergic acid reactions. He had not been a lysergic acid subject himself. This psychiatrist attempted psychotherapy with nine subjects.

Interview with the first two of these nine subjects (Subjects 7 and 8) took place in the presence of two sensitive, alert observers whose purpose it was to record the interaction process between therapist and subject. In each case, these subjects impressed the therapist as having the washed-out appearance of dying persons who had lost all hope. This appearance instilled in the therapist a strong sense of urgency, which was accompanied by a feeling of the need to proceed gingerly, lest he have a damaging effect on the subject through his own sense of alarm. He explored surface phenomena by calling them to the attention of the subject and pursued his responses to a deeper and more intimate level whenever the subject showed signs of increased activity in word or action. Toward the end of about an hour's interview, these subjects, in each case, showed a definite change objectively and subjectively in the direction of less feeling of distress and in better organization of verbal production. In the first subject, the change took place after reaching a climax of weeping. In the second, the change was marked by a rush of sensation of warmth over the skin of the chest. With the first subject, the content of the verbal interchange was largely about ideas. In both cases, the therapist gave an account of his own thoughts and feelings about the subject's appearance and

statements, and sought to help the subject to conceptualize in words his own thoughts and feelings.

With the third and fourth subjects (Nos. 9 and 10) interviewed by psychiatrist J. S. B., the settings of the interviews were marked by the presence of three or four curious onlookers, in addition to the assigned observers. The therapist was obliged in both cases to interrupt a continuing verbal exchange between the subject and other persons present. The third subject evaded the attempts of the therapist to reach her and became uneasier with each question he asked or each remark he made. The fourth subject greeted the therapist with a facetious, devaluating remark and gave his attention to the others present in the room. Both the third and fourth subjects left the therapist to see other people a few minutes after his arrival.

Psychiatrist J. S. B.'s fifth subject (No. 11) was interviewed in the presence of one observer. Early in the interview, two interruptions occurred, during which the subject spoke to the person involved. He was from the outset hostile, teasing, and at times offensive in his remarks to the therapist. Fitful giggling also occurred. His behavior resembled most that of a maniac patient. A remark by the therapist to the effect that he was being carried away by himself was followed by a momentary slowing down, accompanied by a dejected facial expression. This was followed by a return to rapid, intense speech about his childhood and family. From this point forward, his thoughts were well organized. Throughout the interview the therapist did little more than serve as the occasion for the subject to assert himself. In view of the subject's high morale and well-organized thought, the therapist concluded that the subject was counteracting the effects of lysergic acid by exploiting its effect of decreasing repression as an occasion for catharsis, and in so doing was opening more neural circuits. In short, the subject was acting as his own therapist.

Psychiatrist J. S. B.'s sixth subject (No. 12) was interviewed alone while undergoing polygraph study. He presented a picture of dreamy confusion with little distress. His thoughts wandered frequently and would not remain organized around a central theme until the therapist asked questions about his present everyday relations with people. From this point on, the subject remained coherent as long as the conversation revolved around his girl-friend and his mother. There was improvement in the patient's thinking during the interview, but no clear-cut change in his psychophysiological status.

The seventh subject (No. 13) was also interviewed alone while undergoing polygraph study. This subject appeared to be in a pleasant, amused, dreamy state. He was curious about the therapist's purpose in interviewing him and incredulous that he could be helped to feel better or think better with psychological help. He was resigned to the effects of lysergic acid and was willing to wait for them to wear off.

The eighth subject (No. 14) was interviewed in the presence of one observer. This subject appeared to be perplexed and uneasy, but not greatly distressed. The outstanding feature of this interview was that the subject could not see the therapist's face clearly and described it as constantly changing in a wave-like fashion, although the observer's face appeared perfectly normal to him. He was also preoccupied with the therapist's Germanic name and expressed a fear and hatred of Germans. There was little change of note until the topic of conversation shifted to the subject's wife and father-in-law, who is a German refugee. Considerable resentment was expressed toward the father-in-law. There was little change noted in the patient's behavior during the interview, although the therapist resorted to prodding to elicit direct expression of hostility toward him. The most significant change of note occurred after the interview, when the subject met a member of the research team whose name and accent are German and addressed him with open hostility.

The ninth subject (No. 15) was seen by the therapist in response to an emergency call, due to the subject's extreme distress. His face was flushed, pupils were dilated widely, and pulse was rapid and bounding. He was greatly confused and unable to express himself coherently. The therapist's reaction to this subject was that of physician to an acutely ill patient. Direct questions were put to the patient which disclosed that he was badly frightened, and convinced that his confusion and miserable subjective state would never cease. The subject was taken to a bed and told to lie down. After a brief physical examination, the therapist assured the subject in a forceful manner that the effects of the lysergic acid would wear off in a few more hours. He calmed down after a few minutes and then got up from the bed and went for a walk with one of the research team.

At the end of the respective interview periods, three subjects (Nos. 7, 8, 15) showed definite improvement in their feeling of well-being and in their objective behavior. With all of these subjects, the therapist was strongly motivated to help them by the feeling of alarm and urgency in himself which was aroused by the subject's acutely ill appearance. The content of the interviews with these subjects revolved around the immediate situation. The setting in which these interviews took place was one in which the observers also showed a serious and positive interest in the subjects' welfare and respect for the therapist's efforts. Two of these subjects were acquaintances of the thera-

pist; one (No. 15) was a complete stranger to him.

In two of the interviews, the subjects (Nos. 9 and 10) were surrounded by a coterie of onlookers, who were already conversing with the subjects. The therapist was both annoyed by their distracting influence and impressed with the pointlessness of his efforts. Both subjects were acquaintances of the therapist.

In two other interviews (with Subjects 12 and 13) there was little that distinguished them from routine psychiatric interviews with new patients. The interviews were information-gathering and probing in character. Both of these subjects talked most freely about their resentments and grievances in their present life situation. Both were a little better organized in their thinking at the end of the interview period. The therapist had no previous acquaintanceship with these subjects.

In two other interviews the subjects (Nos. 11 and 14) declined or denied the need for help from the therapist. One subject (No. 11) talked largely about his family background; the other subject (No. 14) gave brief answers to direct questions and produced almost no organized verbal material. Both claimed to be feeling no particular distress. Both were acquaintances of the therapist.

Comment

The collective experience of the psychotherapists who sought to alter the course of lysergic acid psychosis brought to light the fact that relief of symptoms was limited to those cases in which the therapeutic interview occurred on an impromptu basis. Discussion among the therapists disclosed that the impromptu cases were those in which the therapists acted on an impulse to take care of an acute emergency. The emergency interviews were unlike the usual scheduled interview in that they were attended by a greater degree of spontaneity on the part of the therapists and were largely disorganized and unstructured. Discussion with the subjects several days after the lysergic acid experiment yielded the added information that both the investigative and the reticent therapist made symptoms worse, while the "self-revealing" therapist, who openly discussed his own experiences by comparing them with those of the subject, was able to give the latter a greater sense of reality and security.

The circumstance that four of the therapists had themselves taken lysergic acid was probably a significant factor in prompting them to report personal experiences in therapeutic interviews with lysergic acid subjects. The one therapist who had not taken lysergic acid reported his experiences of other disturbing emotional experiences. He did this partly out of a desire to learn the effects of lysergic acid by making comparisons. His chief effort was to help the subject by providing him with descriptions of experience which he could accept or reject as analogous to his own.

The effectiveness of spontaneity in the psychotherapy of lysergic acid psychosis, as observed in this study, suggests that the position or pose taken by the therapist with respect to his patient is as important in determining the effect of therapy as the therapist's knowledge of psychodynamics and of himself. The capacity of the therapist to empathsize and identify with his patient is generally recognized as playing a positive role in therapy. Spontaneity in therapy may be secondary to one's capacity to identify with a given patient. This was probably the case in several instances in this study. In other instances, spontaneity was not incident to identifying with the subject, but was recognized as indicated in view of the subject's situation. Here the therapist's spontaneity appeared to be a prerequisite for the subject to attain a basis for identification with the therapist.

The therapist may, on the other hand, adopt the position that he functions as an impersonal and neutral spokesman of mental science and possesses means for objective appraisal of the patient which are derived from authoritative sources outside himself. By adopting this position, the therapist forces the patient to choose between the alternatives of rejecting the therapist altogether, thus clinging to his own interpretation of himself, or of accepting the therapist as the voice of objectivity and thereby discarding not only his own interpretation of himself but also his sense of

integrity and self-esteem. The therapist who takes such a position as his point of departure in communicating with the patient leaves out of account everything that is beyond his knowledge which plays a part in determining both his own and his patient's thoughts, feelings, and behavior. In so doing, he acts as if he were as objective as a surgeon suturing a laceration, when, in point of fact, the margin of knowledge he possesses over that possessed by his patient is relatively small and does not endow him with objectivity.

By acting as though he were actually objective, when he is not, the therapist burdens the patient with incongruous, ambiguous, or self-contradictory communications, which derive from the discrepancy between his not wholly concealed subjective responses and his hypothetical objectivity or objective neutrality.

An alternative position which may be taken by the therapist is that which was adopted in our attempt to alleviate symptoms of lysergic acid psychosis by means of psychotherapy. This position is one in which the therapist allows himself to react subjectively but regards his effort to help as empirical research, in which he and the subject collaborate by pooling their individual experiences, including their experiences of each other. The value to the patient of this procedure is assumed to derive from what the two individuals learn together which adds to the self-knowledge of each. A value of greater importance which accrues to the patient, to the extent that he realizes it, is the discovery that he is not alone in suffering from the problems of subjectivity. An example of performance based on the position of subjective orientation is afforded by one of the therapists who was confronted by the problem of mutism and expressionlessness in some of his subjects. He assumed that this behavior was evidence that the subjects regarded him as a dangerous enemy of superior knowledge, to whom he dared not reveal anything of himself. The therapist tried several ways of dealing with this problem. He sat in silence and waited for the subject to speak; he left the subject several times and returned again. None of these methods met the issue squarely, which had to be met from the subject's point of view, namely, that the therapist reveal himself first and provide the subject the opportunity to evaluate him as trustworthy or untrustworthy. The question then was: How was the therapist to reveal himself? The method adopted in this case was that the therapist imparted to the subject his own stream of thought and associations as faithfully as he himself could tolerate. The content of the stream of thought included the therapist's reactions to the subject's appearance and actions, and also, when they occurred, to his verbal productions. He reacted, in short, subjectively to the patient out of his total experience with people, including his experience as a psychiatrist. By allowing the basis of his relationship with the subject to be fully subjective, he placed himself on an equal footing with the subject; that is, his mental operations and verbalizations occurred within the same frame of reference with respect to the subject as did the subject's mental operations and verbalizations with respect to him. This mode of discourse was successful in six of the nine subjects the therapist sought to help.

Conclusion

The observation of symptom alleviation in lysergic acid psychosis in response to psychotherapy based on communication by the therapist of his subjective reactions to the subject strongly suggests that empirical trial-and-error research in psychotherapy is worthy of exploration. A therapeutic armamentarium could feasibly be accumulated by systematic application of such a method, which would supplement psychotherapy based on special theoretical considerations. It is of historical interest that the first half-century of psychiatry as an independent medical discipline did witness the

collection of an empirically derived psychotherapeutic armamentarium. It was discredited and abandoned about 75 years ago on the grounds that "insanity" was a disease of brain tissue.

Today our conception of psychodynamics, psychopathology, and the requirements for recovery from mental disorders tends to minimize the probability that research aimed toward discovery of an armamentarium of corrective emotional experiences would be successful. There are, on the other hand, indications on the basis of psychodynamics that electric shock and insulin coma are effective as corrective emotional experiences, and not solely as agents of physiological change. The same could be said of occupational and recreational therapy.

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Books

BOOK REVIEWS

Chronic Schizophrenia. By Thomas Freeman, John L. Cameron, and Andrew McGhie, with a preface by Anna Freud and a foreword by T. Ferguson Rodger. Price, $4.00. Pp. 158. International Universities Press, Inc., 227 W. 13th St., New York 11, 1958.

As Anna Freud points out in her preface, "It is a special merit of this book that it offers more than the sober title leads us to expect." The monograph is devoted to a clinical, interpretative, and therapeutic study of chronic schizophrenia within the framework of Freudian psychoanalysis. However, the authors make special reference to the theories and clinical publications of Federn. During the two years of their study, the authors employed three interrelated methods. They began with an attempt to influence their chronic patients by means of group psychotherapy but came to the conclusion that there was no evidence of group formation and that the patients were still behaving as a number of isolated individuals. They state that, in retrospect, at the beginning of their work they lacked experience and understanding of chronic schizophrenia, so that they overestimated the value of the spoken word for these patients. The second method which they used to observe chronic schizophrenic patients was to place a number of chronic female patients in a pleasant room with two nurses and to observe the impact of the new environment and the closer contact between nurses and patients. The third method of observation consisted in one of the investigators spending several hours a day in a female ward, sitting in the same seat, never interfering in any direct way with the ward management, but not rejecting any approach by patients or staff. He sat in at the nurses' tea break, where he then discussed with the nurses the events in the ward, much as was done at the weekly staff meetings.

The first portion of the book is largely theoretical, dealing with a theory of mental functioning and an excellent review of the psychopathology of schizophrenia. The authors then discuss, under several headings, the confusion of identity, disturbances in perception, disturbances of thinking, disturbances of memory—all on the basis of clinical observations of their patient-subjects. The last section of the book is devoted to a discussion of treatment of chronic schizophrenia. Their basic principle is that the condition of schizophrenia is one in which the normal continuum between the ego and the outside world is grossly disturbed, and they suggest that the schizophrenic suffers from a deficiency of "ego feeling," or the capacity of self-experience. They believe that all other behavioral manifestations of the illness are but necessary concomitants. The authors state that no activity occurring within a social structure such as a mental hospital can be considered in isolation, and they rely most heavily on continuity and consistency of contact between nurse and patient. This is achieved by training of the psychiatric nurse, not through lectures and seminars but through the medium of direct experience in the actual situation.

Each of the patients whose descriptions are interpolated throughout the whole book are described in detail in an appendix. There is an excellent bibliography on the literature of chronic schizophrenia, and the index is quite adequate.

Those psychiatrists who are interested in the psychosocial approach to the problem of chronic schizophrenics in the mental institution should read this brief volume very carefully. It contains a tremendous fund of knowledge and very well-written statements of the authors' actual experiences with their own form of treatment. This book should offer a useful antidote to the grosser, and sometimes ruthless, approach by some American psychiatrists using either physical or verbal onslaughts on their patients.

ROY R. GRINKER, M.D.

Psycho-Endocrinology. Max Reiss, M.D., D.Sc., Editor. Price not stated. Pp. 208. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1958.

"Psychoendocrinology" and "neuroendocrinology" are recently coined words describing the functional and structural interrelationships of the central nervous system and the endocrine glands. A Symposium on Psycho-Endocrinology was held at the Second International Congress for Psychiatry, and in the 1957, present volume is a collection of the papers presented at that symposium.

The most interesting paper is the first, which provides a theoretical framework, not only for the subsequent papers but for the field as a whole. In this introduction, Max Reiss char-

acterizes and discusses three elements concerned in the development of mental diseases: personality pattern, emergency situation, and endocrine equilibrium. Since there is evidence that the anterior pituitary is at least partly controlled by the hypothalamus, which is connected to other areas of the brain, and since the target-gland hormones, in turn, can act on the brain, endocrine disturbances, if present in a patient undergoing psychotherapy, should be diagnosed adequately and treated in the hope of improving psychopathological symptoms. Reiss (properly it seems) rules out "any hope of ever finding a special hormone therapy for depression, schizophrenia, etc.," and, instead, states that hormone treatment in psychiatry (and it is hoped also in other areas of medicine!) "can only be attempted on the basis of a preceding definition of the endocrine status of the patient."

Most of the subsequent papers describe clinical experiences with various endocrine malfunctions in mentally disturbed patients. Measurement of thyroid, adrenocortical, and/or gonadal functions in various patients is discussed, and rational therapeutic measures are described in specific case histories. The final three papers deal with experimental investigations of "psychoendocrine" relationships. Richter discusses abnormal behavior cycles in rats and patients; Reiss discusses the effects of chlorpromazine on adrenal, thyroid, and gonadal function in rats, and Sloane, Saffran, and Cleghorn describe the effects of chlorpromazine on the adrenal response to corticotropin in psychoneurotic patients.

The book is well worth reading, not only by psychiatrists interested in the somatic concomitants of mental disease but also by experimental endocrinologists, who too often neglect to make simple behavioral observations of their animals while performing complex analyses of histological, physiological, and biochemical variables.

NEENA B. SCHWARTZ, Ph.D.

Objective Approaches to Treatment in Psychiatry. By Leo Alexander. American Lecture Series No. 327. Price not given. Pp. 139, with 23 figures. Charles C Thomas, Publisher, Springfield, Ill., 1958.

The production of abnormal mental states by drugs and other means, and their abolition by other drugs, the ability to prognosticate on the basis of physiologic responses to the injection of certain chemicals, the recognition of the parts played by excitation and inhibition in complex emotional states, and the factor of the physician as a guide in the psychotherapeutic relationship—all these are surveyed with as much objectivity as possible in this easy-to-read volume.

From the practical standpoint, the author shows how Funkenstein's epinephrine-methacholine (Mecholyl) test will point almost unerringly to the method most likely to secure a favorable response to therapy. Even more important, however, is the recognition of depression as a transmarginal inhibitory state, the product of insupportable anxiety. When the psychiatrist turns his attention to the fundamental processes, instead of being preoccupied by the symptomatic expressions of the disorder (which Alexander likens to the final common path of classic reflexology), he becomes more concerned with rectifying the disordered elements by a variety of means at his disposal, methods that have been established by experimental means as altering in one way or another the fundamental physiologic patterns.

The reciprocal relationship between anxiety and depression is clearly demonstrated. By stimulation through nonconvulsive electric treatments, by drugs, and by psychologic methods, anxiety can be aroused beyond tolerable limits to the point of inhibition, resulting in depression. Convulsive treatment, on the other hand, suppresses the overwhelming anxiety manifested as depression and restores the patient to a state where the residual anxiety will respond to other methods.

The Funkenstein test can also guide the psychiatrist in the administration of drugs, either of the tranquilizing or of the stimulating group. The tranquilizers "appear to suppress the primary, epinephrine-precipitable, subcortical—warning—or tension—anxiety, while exerting only an indirect influence on its secondary disorganizing effects, namely, panic or depression." Drug therapy is hence most useful in excited states that are naturally of short duration. Continuation of the drug after the manic stage has passed may result in depression. Since the tranquilizing drugs enhance suggestibility, they are useful in the psychotherapeutic situation where progress is blocked by anxiety. In chronic psychotic patients they suppress symptoms to a variable degree without bringing about actual recovery.

Among the other drugs, the combination of meprobamate, 0.4 gm., and benactyzine, 1 mg., relieves anxiety plus depression in patients who might otherwise need electroshock therapy. The elevation of the psychic pain threshold seems to be the key in this situation.

Frontal lobotomy is reserved for those patients with intractable suffering. "The advantage of the operation in such chronic cases is that the successfully lobotomized patient becomes truly free, able to regulate his own life, a state which the patient on maintenance drug therapy can never achieve." The operation works apparently by reducing the number of neuronal circuits connecting higher with lower centers.

Psychotherapy is viewed in the Pavlovian frame of reference as a process of extinction conditioning, by means of a repetition of signals without reinforcement, in the supportive presence of the physician. Reevocation of feelings to the point of emotional abreaction is a necessary feature, sometimes followed by exacerbation before the emotional response finally dies out. In the process of working through, psychotherapy is considerd as a learning process, aided by suggestion, mimesis of the therapist, and identification with him. Uncovering narcissism, hostility, and other disturbing aspects inherent in everyone, but exaggerated in the sick person, may lead to intolerable anxiety with dangerous depression. Concomitant treatment of the anxiety and depression renders the patient better able to accept himself and to profit from the therapeutic relationship. "The therapeutic work must then be directed toward restoring the compensating forces rather than toward the essentially normal underlying function that has found misadapted expression through illness."

WALTER FREEMAN, M.D.

Psychotherapy of Chronic Schizophrenic Patients. Edited by Carl Whitaker and Thomas Malone. Price, $5.00. Pp. IX + 219. Little, Brown & Company, 34 Beacon St., Boston 6, 1958.

This volume represents an attempt on the part of seven psychiatrists and one anthropologist to report a series of bull sessions devoted to discussing their extensive clinical experience with schizophrenia, and some summarization by the editor. The discussion roams from diagnosis, dynamics, communication, effect, cause, and cure to the special problems of the therapist treating severely disturbed patients. Addressing themselves to the question of psychosis, this group seems to go through stages paralleling the experiencing of the "therapeutic psychosis," as described by Whitaker and Malone in "The Roots of Psychotherapy" (New York, The Blakiston Company, 1953). In the course of their ramblings, everything becoms psychosis: All children are born psychotic; all therapists are psychotic or have a need to become more psychotic; all patients need to become more psychotic before they can become less psychotic. By immersing themselves in what seems to be psychopathologic exchange, where no one answers anyone else, where each is associating freely, frequently without reference to what has been said by the previous speaker, the participants and the reader are led into confusion and chaos. In the beginning some members hold out for rationality, criteria, science, and sense, but they cannot maintain this reality-bound position under the constant confrontation with nonsense, fragmentation, word salad, and paralogisms.

The following is an example of the kind of free-associative material that is offered to professional colleagues interested in treating schizophrenic patients.

"Rosen: Does the patient make me grow? Me, as a person?

"Malone: Yes, more as a person.

"Rosen: I don't think I should grow any more. (Laughter) Hit him below the belt. He caught me in the diaphragm. He stinks!

"Malone: Get rid of your diaphragm and you might get pregnant (page 170)."

With rapid strides the group moves more and more to an acceptance of the precepts of the irrational psychotherapy of the team of Whitaker, Malone, and Warkentin. The members reject objective criteria, history, science, causation, reality, and culture and affirm the desirability of illusion, fantasy, subjectivity, feeling, miracle. Their denial of reason leads to such a fantastic conclusion as that the goal of therapy for therapist and patient is change, and it does not matter in what direction the change may be. "Malone: We agreed that it changes you personally to treat a schizophrenic patient, without making any judgment on the direction of the change. We agree about that? (Everyone agreed.) (page 170)."

The position is promoted that therapy is advanced to the degree that the therapist can express the most regressed subjective psychopathology. The primary processes in therapist and patient are defined as being healthier, more useful, more creative, more loving, more socializing than ego functioning. The best way to maintain one's mental health, it is said, is to be unconscious. In view of the rejection of consciousness as a legitimate compound of the therapeutic experience, the recommendation is made for a second administrative therapist, so that the "real" therapist may remain in bilateral unconscious "relationship" to the patient. The psychotic

state is projected as protective, immunizing, curative. There is something out of this world about their presentation, in which the differences between schizophrenic patient and therapist, between schizophrenic patient and husband or wife of the therapist, between schizophrenic patient and the therapist's colleagues are all denied. This leveling in pathology seems to be the objective of the activities propounded by this group. They attempt to deny all differences between patient and therapist, therapy and living, reality and illusion.

Instead of offering the reader some rational basis for dealing with the very complicated problem of treating the chronic schizophrenic patient, they insist upon the value only of subjectivity, the therapist's expressing personal affect, which is unique, projective, and incommunicable to the patient. The therapist, like the "changing" patient, moves into greater individual isolation. The more unconscious the therapist is with himself, with his colleagues and in the totality of his interpersonal relations, the more mature (in their sense) he becomes. The good therapist, in their view, is one who is therapist-oriented, for only his needs are important. Patient-oriented therapy is bad for therapist and patient as they see it. Their rationalization for this position is that the patient (who is the therapist) is benefited by such a procedure. It is our impression that no one benefits by such acting out, isolation, fragmentation, confusion, and aggression. The members of the panel rationalize acts of aggression against patients in the statement that as a therapist, "You can't hurt the patient; you can only hurt yourself (page 178)."

They recommend the gratification of archaic needs rather than moving the patient toward current constructive alternatives. The following quotation gives us a sample of the infantilizing "therapeutic" maneuvers, which include rocking and bottle feeding, spanking and violent manhandling, silence and falling asleep; all of these activities on the part of this kind of therapist are directed toward bringing the patient closer to reality.

"Rosen: After great devotion of time and thought to some phase of treatment, like feeding him the bottle day and night on a regular schedule while a lullaby is turned on with a phonograph, there may come a point where the patient reaches close to reality (page 193)."

There seems to be world-wide trends in the culture in general, and in psychotherapy in particular, to reject reason, health, rationality, and science and to glorify mysticism, subjectivity, aggression, and unconsciousness. This book is an example of the trend. It denies objectivity and intelligence, makes outer reality a projection of unconscious processes, promotes paranormal, id-to-id pseudocommunication and seeks meaning in life "beyond survival." What we are offered here is in the irrational tradition of Zen-Buddhism and existentialism in psychotherapy and "The Roots of Psychotherapy" by Whitaker and Malone.

ALEXANDER WOLF, M.D.
EMANUEL K. SCHWARTZ, Ph.D., D.S.Sc.

Otto Rank—A Biographical Study Based on Notebooks, Letters, Collected Writings, Therapeutic Achievements and Personal Associations. By Jessie Taft, Ph.D. Price, $6.50. Pp. 299. The Julian Press, Inc., 80 E. 11th St., New York 3, 1958.

In the foreword, Taft states the purpose of the book as follows: "To present something about Rank as a genius, an artist in his own right, not as a disciple of Freud but in terms of his own self-development; the inestimable value for him of his finding of Freud and the inner necessity (for his genius) as well as the personal tragedy of his separation from the Freudian group."

The book is divided into four chapters, each covering significant periods of Rank's life and the influence each had on the one to follow. The first chapter, "The Early Years," draws its content from the four "daybooks," which were started in 1903, when Rank was 19 years of age, and continued up to 1905, when his momentous meeting with Freud occurred. The second chapter is devoted to the years of association with Freud and the small inner circle of disciples charged with the responsibility of spreading Freud's revolutionary concepts. The content of this period is drawn mainly from the original and unpublished letters between Freud and Rank, tied together by comments and interpretations by the author, whose close association with Rank began in 1926 and continued up to his death, in 1939. The third chapter, "The Years of Fulfillment," draws its content from letters between Taft and Rank and the author's account of Rank's teaching and therapeutic experiences in New York, Philadelphia, and Paris. This chapter includes Rank's abstract of his own paper given at the International Conference in Washington in 1930. This occasion brought Rank before an American audience and offered his severe critics the opportunity to attack him, and they took full advantage of it. The abstract is well worth reading today. On this occasion Rank openly differs from Freudian theory

(pages 147-151). The final chapter, "Otto Rank, Artist," is a highly condensed summarization of Rank's major contributions, with excerpts from "Art and Artist" and his posthumous book, "Beyond Psychology."

This book, particularly the first two and the final chapters, should be widely read. It has value far beyond the study of the evolution of Rank's personality. In being that, it is the story of an ever-repeating process of self-development—a child becomes different from its parent; the pupil moves beyond the teacher; the disciple to nourish the creative quality becomes more than a follower of the master. Alan Gregg once said: "Loneliness is one price of greatness." Freud and Rank each found in the other the satisfaction of a great human need. Each suffered in the inevitable separation. But Freud had the affirmation of his theories from an ever-widening group of students. Rank, in his isolation, had to affirm himself out of his inner resources (page 272). While he suffered and went through periods of deep depression, he, as the author brings out, made creative use of his suffering.

During the period that Rank was a key person in the Committee and, together with Sachs, had the advantage of daily association with the "Professor," Freud recognized, and in many ways encouraged, Rank's capacity for independent thinking. At the same time, he considered that Rank was insufficiently systematic and strove to help him remedy what seemed to Freud one-sided or extreme conclusions. In one letter Freud says: "I have the fear that through my criticism, I will hamper their independence because I myself am so slow to take on anything new and I work away in my own province." (page 75) Freud then proceeds to give Rank constructive criticism and adds: "With such valuable content the work lacks the inner structure through which the reader would be enabled to grasp the whole."

Freud recognized through these comments Rank's tendency to be ahead of his readers. Taft brings out this same tendency, which made it difficult for his readers and listeners to understand him (page 284). Rank, with his artist quality, tended to make his ideas total and to universalize them. Freud once told him: "Throw an easier fragment to the Congress." Rank had great difficulty in doing this.

The person deviating from the current idiom always has a rough time. Rank deviated from the group who were seeking to establish Freud's theories, which at that time were being attacked by those who regarded Freud as a deviationist, and therefore a threat to established ways of thinking. Rank was a member of that inner circle who tried to maintain a tight "togetherness." So when Rank revealed his independent thinking by suddenly producing in finished form "The Trauma of Birth," he threatened the cohesiveness of the group, who had set themselves up as "saviors of the psychoanalytic movement" (page 102). Freud was deeply hurt by Rank's assertion that "the psychoanalytic movement as such is a fiction," and by such statements Rank added fuel to the rancor engendered by his independence. But Freud, in responding to Rank, says about the "Trauma of Birth": "In no case do you have to be ashamed of your product, rich in spirit and content which brings new and valuable ideas, even to the critics." (page 105).

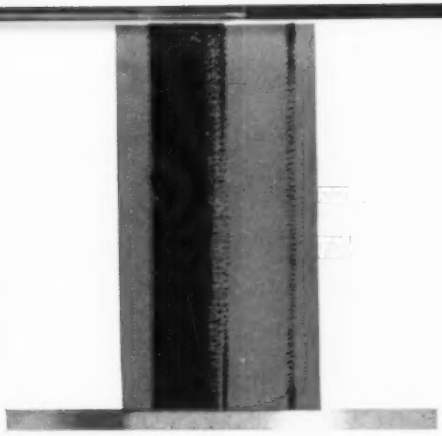
Rank has been one of the central objects upon whom has been focused much hatred. In many circles, particularly among many ardent psychoanalysts, he has been regarded as a traitor, an ingrate who turned against the most important person in his life. It is an amazing phenomenon that such blasts of feeling are aroused in the realm of ideas and concepts. The controversy engendered moved out of the realm of scientific exploration when it became so personalized. This material reveals an important fact. Freud was the most understanding of the early group. He tried to keep the controversy where it belonged—on differences in their theoretical points of view. But others, particularly Jones, fed the fires that made the issues so personal and had to explain Rank's deviations by calling him neurotic.

The most creative results of a master's teaching is the encouragement and support he can give to the pupil to become himself and not an imitation. Freud himself was a creative rebel and aroused strenuous opposition. Rank also was a creative rebel. But science and art are enriched by those who have the courage to carve new pathways and seek new knowledge. Whether one agrees with the new is beside the point. The more important element in progress is a deep respect for difference—a respect for one's own contributions, which must always respect the right and need of others to differ.

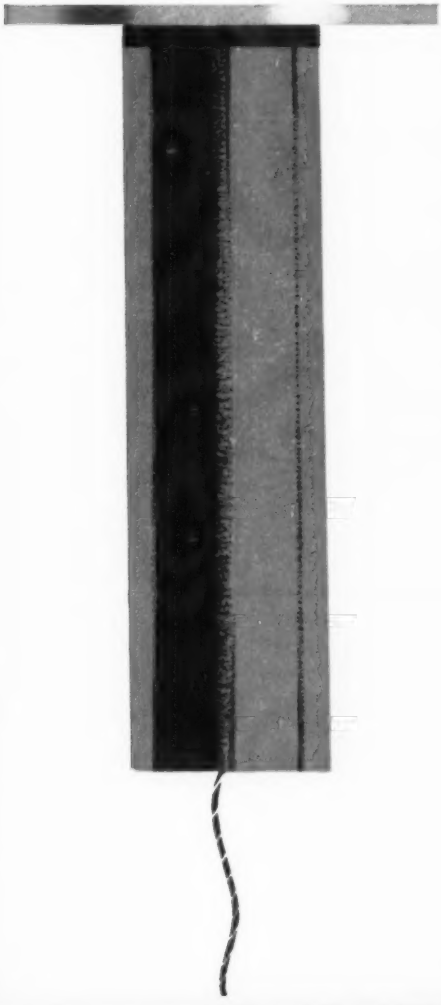
The book is written by one who was Rank's most vigorous and thoughtful follower in the United States. It is full of personal impressions and memories, but she maintains an objective tone throughout and the book should throw new light on one of the most controversial figures in the history of psychoanalysis.

There is appended a complete list of Rank's publications. There is no index.

FREDERICK H. ALLEN, M.D.



'Compazine' highly effective with ECT



Twenty-eight acute schizophrenics received a combination of 'Compazine' and electroconvulsive therapy. Twenty-six showed marked improvement. Patients were calm and less apprehensive between treatments, and they were readily accessible for psychotherapy. No episodes of vasomotor collapse occurred.[1]

*Compazine**

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1. Wilcox, F.: Dis. Nerv. System *19*:104 (Apr.) 1958.

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References:
1. Bowes, H. A.: Am. J. Psychiat. *113*:530 (Dec.) 1956.
2. Bruckman, N., *et al.*: Am. J. Psychiat. *114*:262 (Oct.) 1957
3. MacGregor, J. M.: South African M. J. *30*:1108 (Nov. 17) 1956. 4. Sarwer-Foner, G. J., and Koranyi, E. K.: Canad M. A. J. *77*:450 (Sept. 1) 1957

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1. Alexander, L.: Chemotherapy of depression.—Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. **166**:1019, March 1, 1958. 2. Current personal communications, in the files of Wallace Laboratories.

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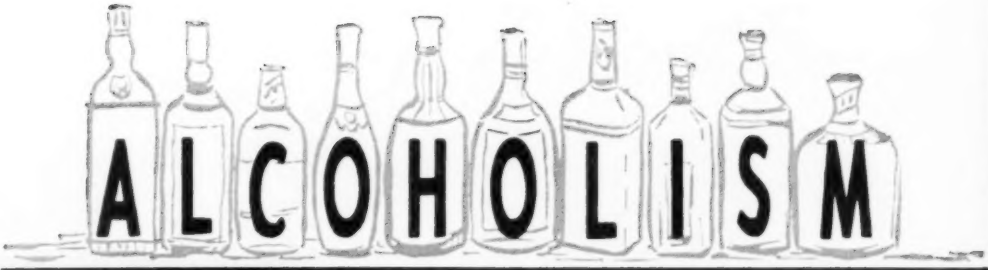

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